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BRITISH JOURNAL OF ANAESTHESIA

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EDITORIAL

THE "BRITISH JOURNAL OF ANAESTHESIA" AND "ANAESTHESIA"

At the Annual Meeting of the Association of Anaesthetists held in Southport in October 1959, the Honorary Treasurer had to present a balance sheet which, for the first time, showed a considerable excess of expenditure over income. This was to a large extent due to a fall in the income from the journal *Anaesthesia*. It was appreciated that this was mainly attributable to the fact that a larger than usual number of subscriptions to the Journal were outstanding at the time of closing the year's accounts. Nevertheless the Council of the Association was anxious about the situation and a sub-committee was asked to look into the matter. This sub-committee confirmed that it was likely that this loss would be offset to some extent by a considerable profit this year—a forecast which has been proved correct. However the sub-committee had wide terms of reference and felt that something would be gained by examining the whole position of journals of anaesthesia in this country. It realized that there was much to be said for one journal representative of the best work and it decided to explore with the Board of Management of the *British Journal of Anaesthesia* the possibility and desirability of a merger. The Board of Management and the publishers of the *British Journal of Anaesthesia* showed that they were willing to co-operate and suggested conditions on which an amalgamation of the two journals might be achieved. Although many in the Council of the Association saw the advantages of one journal, there were misgivings on the effect of the greatly increased subscription which would become necessary, and there was doubt as to the practicability of the proposed editorial arrangement. Finally, there was a minority who considered that it was desirable to have two journals of anaesthesia and that competition was a good thing.

The Council considered that in the absence of unanimous enthusiasm for the move it would be undesirable to proceed further.

It is hoped that both these journals will continue to go from strength to strength and remain worthy of the high standard of the specialty in this country.

Brit. J. Anaesth. (1959), **31**, 518

THE PROPERTIES OF THE ANAESTHETIC SUBSTANCE 1:1:2-TRIFLUORO-1:2-DICHLOROETHANE

BY

J. H. BURN, H. G. EPSTEIN AND P. J. GOODFORD

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THE Committee on Nonexplosive Anaesthetics of the Medical Research Council is concerned with the task of finding a nonexplosive anaesthetic which is safe to use. Compounds have been prepared in Birmingham University by Professor M. Stacey and his colleagues Professor J. C. Tatlow and Dr. G. Fuller. These compounds have been given a preliminary test, to see if they possessed anaesthetic properties, by Dr. T. H. S. Burns of St. Thomas's Hospital and Dr. J. M. Hall of Guy's Hospital. Six of the compounds selected in this way were sent to us for further examination. This account of the properties of the compounds forms a Report to the Committee.

STRUCTURE OF THE COMPOUNDS

Three of the compounds were derivatives of ethane; their formulae were

Compound A $CFCl_2.CFCl_2$
" B $CF_2Cl.CFCl_2$
" C $CF_2Cl.CHClF$

Three of the compounds were ethers; their formulae were

Compound D $CFHCl.CF_2—O—CH_3$
" E $CFHCl.CF_2—O—CH_2.CH_3$
" F $CFHCl.CF_2—O—CH(CH_3)_2$

OBSERVATIONS ON MICE

For the examination in mice we have used an apparatus essentially similar to that described by Raventós (1956). The anaesthetic was driven into a vaporizing chamber at a known rate. In the chamber which was immersed in a water bath at the boiling point of the anaesthetic, it met a current of air also flowing at a known rate; thus a current of air containing a known percentage of anaesthetic was obtained. This mixture then passed into a larger chamber in which a group of 10 mice were placed. The effect on the mice, premedicated with atropine 0.2 mg/kg body weight given intraperitoneally, was observed during a period which might be 15, 30 or 60 minutes; the number which were unable to right themselves and the number which were unaffected by a pinch at the base of the tail were recorded. On being taken from the chamber the mice were observed during 2 weeks to see if any of them died.

The results for compounds A and B have already been published (Burn, 1959). Compared with ether and with halothane they were both unsatisfactory. For each of them the concentration producing anaesthesia in 50 per cent of the mice was about half the concentration which caused death in 50 per cent of the mice, whereas for ether and for halothane it was only one-third. Moreover, compounds A and B caused initial excitement and convulsions during anaesthesia. Some of the results for compounds D, E and F are set out in table I. Compounds E and F were unsatisfactory because concentrations which produced anaesthesia killed the mice. While compound D did not kill, during induction of anaesthesia it caused excitement and, later, tremors during anaesthesia.

TABLE I

Compound	Concentration % v/v	No. of mice anaesthetized	No. of mice dying	Side effects
D	1.5	9/10 in 30 min	0 out of 10	Initial excitement
E	1.0	2/10 in 30 min	8 out of 10 in 3 days	Tremors
F	2.0	10/10 in 10 min	6 out of 10 in 8 days	Convulsions

TABLE II

Observations on groups of 10 *mice.*

A = number lying on their sides; DA = number not responding to tail pressure; SB = number breathing at less than 60 per min; D = number dead within 1 hr.

Time	Conc. % v/v	Compound C				Ether				Halothane			
		A	DA	SB	D	A	DA	SB	D	A	DA	SB	D
15 min	2									10	10	2	0
15 min	2.5									10	10	4	0
15 min	3	1	0	0	0	0	0	0	0	10	10	6	3
15 min	4	9	0	0	0	6	0	0	0	10	10	10	3
15 min	6	10	10	1	0	10	9	1	0				
15 min	7	10	10	0	0	10	10	0	0				
30 min	2									10	10	7	0
30 min	2.5									10	10	9	0
30 min	3					2	0	0	0				
30 min	4	10	3	0	0	10	8	1	0				
30 min	6					10	10	5	3				
30 min	7	10	10	2	0	10	10	3	1				
60 min	2									10	10	9	0
60 min	2.5									10	10	10	4
60 min	4	10	6	0	0	10	7	2	0				
60 min	7	10	10	5	0	10	10	10	9				

Compound C in mice.

In contrast to the other substances compound C was satisfactory in tests on mice and was in no way inferior to halothane or ether. The results are given in table II, from which it appears that compound C was similar in potency to ether. However, ether in 6 per cent (v/v) concentration given for 30 min caused 3 out of 10 mice to die, and in 7 per cent concentration for 60 min caused 9 out of 10 mice to die. These deaths were probably due to respiratory obstruction. Compound C in 7 per cent (v/v) concentration for 60 min did not cause any deaths. When compound C was administered the onset of anaesthesia was smooth; no tremors developed in the mice and no excitement was evident. Further tests were carried out on dogs.

OBSERVATIONS ON DOGS

Method.

Compound C was a clear liquid boiling at about 30°C, with a specific gravity of 1.5. A mixture of its vapour with air was prepared in the same way as for the mice. A syringe, driven by a motor, delivered liquid paraffin at a constant rate into a container from which it displaced mercury (fig. 1). The mercury in turn displaced the anaesthetic into a vaporizing chamber immersed in a bath at constant temperature where it met an air stream flowing at a known rate. The mixture was delivered through a chamber, with metal vanes at intervals to ensure thorough mixing, into a main duct leading to the dog. Attached to the side of this duct were two polythene bags each of 60 litres capacity and each separated from the main duct by a large stopcock. The bags were filled with mixtures of different compositions. The mixture could be supplied artificially to the dog by using an Oxford Inflating Bellows (O.I.B.). For this an excess flow of the mixture was utilized and the surplus was spilled. During the usual administration of the anaesthetic when the dog was breathing spontaneously the mixture passed through the O.I.B. to a metal block near the head containing an inlet valve, an outlet valve and a short pipe for a flexible connexion to the endotracheal tube. The inlet valve on the O.I.B. was loaded so that part of the mixture coming from the vaporizing chamber entered one of the polythene storage bags. In this way excessive waste by the valve system was avoided. The outlet pipe from the metal block, which contained the expiratory valve, was connected to a gas clock of the type made by Siebe Gorman. The movement and size of the concertina bag of the O.I.B. gave an indication of the depth of respiration during

FIG. 1

Apparatus for administration of compound C to a dog through a cuffed endotracheal tube. "Hg pump" represents a motor-driven syringe driving liquid paraffin into a receptacle from which mercury is displaced at constant rate. The displaced mercury enters F and drives the liquid anaesthetic into the vaporizing chamber E in which it meets a current of air coming through flowmeter R. The mixture then goes through a mixing chamber M either (*a*) to a 60-litre bag for storage, or (*b*) through an inflating bellows to the dog. The expired air from the dog goes through a gas clock G.

spontaneous breathing. During artificial ventilation the outlet pipe leading to the gas clock was disconnected and the outlet was occluded by a finger while the O.I.B. was worked by hand.

RESULTS

The following observations were made when compound C was administered to dogs either by Dr. R. A. L. Leatherdale or by Dr. J. Parkhouse, both consultant anaesthetists.

Induction of anaesthesia.

In order to observe whether induction with compound C was smooth, two dogs were used. For each experiment a concentration of 14 per cent of compound C was prepared in one bag and a concentration of 7 per cent in the other. The dogs were not given atropine or other injection beforehand. A metal mask lined with a sorbo sponge ring to fit comfortably over the dog's nose was used, the dog being held during the early stages of induction. With both dogs induction of anaesthesia with 15 per cent of compound C was smooth; there was no stage of excitement, there was no salivation and complete muscular relaxation was obtained. Neither dog struggled more than was to be expected from the fact that it was restrained during the first minute or two. The onset of anaesthesia was rapid and breathing continued normally until the dog became completely relaxed. An endotracheal tube was then passed and the mixture was changed from 14 per cent to 7 per cent for maintenance. We had previously given halothane to dogs and found occasional difficulty with respiration at the end of the period of induction. Respiration became rapid and shallow and, in two cases, stopped just after the insertion of the endotracheal tube. With compound C there was no indication of respiratory depression during induction. When the anaesthesia had continued for 5 minutes the anaesthetic was withdrawn. The dog rapidly recovered and was sitting up, in one case after 3 minutes

and in another case after 5 minutes. The dogs were walking around within 12 minutes.

Effect of compound C on respiration.

In order to economize material, anaesthesia was induced in other dogs with ether and was then continued with compound C. In all experiments the respiratory rate and the minute volume were recorded. The effect of compound C was observed for periods up to 70 min; anaesthesia was generally light with 4 per cent but relaxation became complete between 4 per cent and 7 per cent. With these percentages respiration continued normally and quickly responded in rate and depth when anaesthesia was lightened. Table III gives an example of changes in respiration, in which the rate remained steady for 47 min around 60 per min, and the minute volume was not greatly depressed when the concentration of compound C was changed from 4 per cent to 6 per cent.

In one dog the concentration of compound C was raised to 12 per cent, but, even so, respiration continued slowly though it became very shallow. Under 4 per cent compound C the minute volume was 3 litres/min and the rate was 44/min. Under 10 per cent after 5 min the minute volume was 2 litres/min and the rate 36/min, and under 12 per cent after 4 min the minute volume was 1 litre/min and the rate was 20/min. When compound C was removed and the anaesthesia became light, the minute volume was 4.3 litres/min and the rate 48/min.

Effect on blood pressure.

The administration of compound C caused a severe fall in blood pressure in all experiments. An example is seen in figure 2 in which 6 per cent of compound C was given to the dog which was anaesthetized with ether, and therefore had a high systolic pressure of 170 mm. In 3 min the pressure fell to 78 mm Hg and an operation for unilateral nephrectomy was begun. After a further 8 min the concentration of compound C was reduced to 4 per cent (fig. 2b) and kept there until the operation was complete (see "F" fig. 2c). The blood pressure then was 71 mm (fig. 2c) and rose on discontinuing the anaesthetic to 148 mm in 5 min.

Similar observations were made in cats. Figure 3 shows the effect of administering 4 per cent compound C to a cat already anaesthetized with chloralose. The blood pressure fell from 114 to 58 mm Hg in 8 min. d-Tubocurarine (at "1 mg C") had no depressor effect on the blood pressure, and vagal stimulation (V) was ineffective. After the discontinuance of compound C the blood pressure recovered to 98 mm Hg in 9.5 min.

Operations in which anaesthesia was induced with ether.

In two of these dogs in which anaesthesia was induced with ether, operations were performed by Mr. A. J. Gunning, F.R.C.S. In the first operation a concentration of 4 per cent compound C was sufficient for the operation of unilateral nephrectomy to be carried out. At this concentration dragging on the mesentery or manipulation of the viscera caused no reflex movements, and did not modify the blood pressure. The operation was complete in 29 min from the time of administering compound C.

In the second operation, in which the chest was opened and a rib resection was performed, ether was given in 8 per cent concentration at first

TABLE III
Respiratory changes under Compound C

Time min	Anaesthetic	Concentration % v/v	Minute volume litres/min	Respiratory rate/min
	Ether	8	12	92
0	Compound C	4	—	—
14	Compound C	4	7.3	64
24	Compound C	4	7.2	58
25	Compound C	6	—	—
36	Compound C	6	5.9	60
39	Compound C	4	—	—
47	Compound C	4	8.5	68

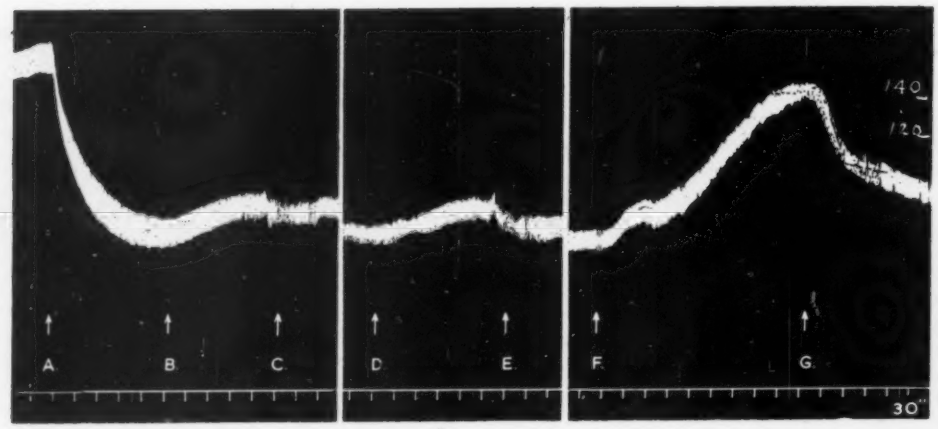

FIG. 2

Record of blood pressure in dog. At A, ether was discontinued and 6 per cent compound C was given. At B an operation for nephrectomy was begun. At C pulling on the mesentery evoked no response. At D 4 per cent compound C was given. At E pulling on the mesentery evoked little response. At F the operation was finished and compound C was discontinued. At G 4 per cent compound C was given to allow removal of artery cannula. Time mark = 30 sec.

and then compound C was given in 6 per cent concentration for a period of 4 min, after which the concentration was reduced to 4 per cent. When the chest was open the respiration was controlled by using the bellows. The operation was completed in 18 min.

Postoperative condition.

The recovery of the dogs, whether surgically operated on or not, was remarkably rapid. Thus the dog (not operated) which was at one stage anaesthetized with 12 per cent compound C held up its head within 4 min of discontinuance of the anaesthetic, and tried to walk in 8 min. It ate its food the same evening and was lively the next morning, passing 260 ml of urine in 24 hours. The condition of the dog on which the rib resection was performed was equally good, though it passed only 15 ml of urine in the first 24 hours; in the second 24 hours it passed 195 ml. It was very lively on the second day, eating well.

Ganglion-blocking action.

Experiments were carried out to determine whether compound C had a blocking action on sympathetic ganglia. The preganglionic fibres of the cervical sympathetic chain of a cat were cut and placed on shielded electrodes. A thread was passed through the edge of the nictitating membrane of the eye and taken by way of pulleys to a lever. A stimulus was applied to the preganglionic fibres and was maintained for several minutes as shown in figure 4b. On application of the stimulus the membrane contracted; the contraction rose to a peak and then declined slightly, to be maintained at a height below the peak. The cat, which had been receiving ventilation with air, was then ventilated with air containing 7 per cent compound C. In 1 min the nictitating membrane relaxed as shown. The anaesthetic was stopped after 1.75 min, and in 1 min more the nictitating membrane contracted again, though it did not reach the former height. When the stimulation stopped the nictitating membrane relaxed.

The vagus nerve was stimulated to see whether vagal impulses were blocked by compound C. Figure 4a shows the result in one experiment on a cat in which vagal stimulation was effective before compound C was administered and was still effective after 7 per cent had been given for 5 min and had caused a fall in blood pressure.

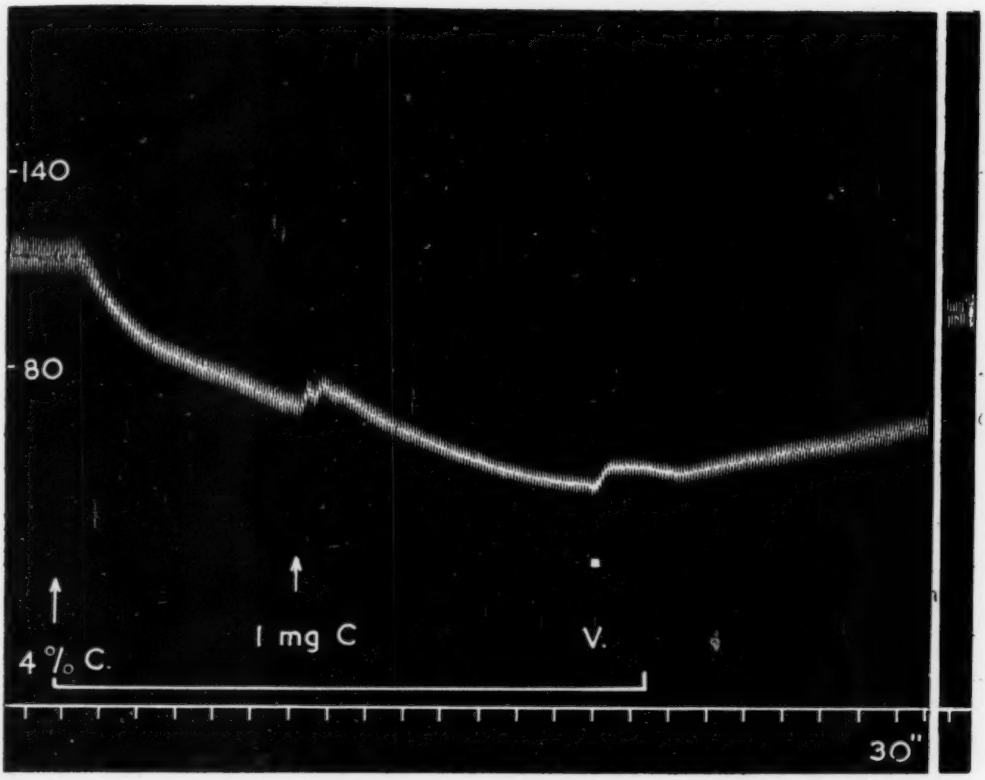

FIG. 3

Record of blood pressure in cat anaesthetized with chloralose. Administration of 4 per cent compound C for 8 min. Injection of 1 mg tubocurarine (1 mg C) did not exert a depressor action. Vagal stimulation (V) was without inhibitory effect.

Similar observations were made in other animals, and only after tubocurarine had been given (fig. 3) in addition to compound C, was vagal stimulation ineffective.

Effect on cardiac output.

Observations were made on the effect of compound C on the cardiac output in the Starling heart-lung preparation of the dog. The output was measured by collecting the blood about to enter the venous reservoir during 15-sec periods. At a given time the lungs were ventilated with a mixture of air and compound C, and the output was measured at intervals. The effect of compound C was compared with that of halothane, observations being made alternately with the one and then with the other. Between each observation the preparation was respired with air for long enough to recover the initial output.

Table IV shows the earlier results in one experiment. The fall in output caused by 4 per cent compound C was very slightly greater than that caused by 1.5 per cent halothane, compound C being administered both before and after halothane. The output is shown as a percentage of the initial output in figure 5. When a higher concentration of compound C, 7 per cent, was given, this diminished the output slightly less than 7 per cent halothane. At that point of the experiment, however, the preparation was beginning to deteriorate due to successive exposures to the

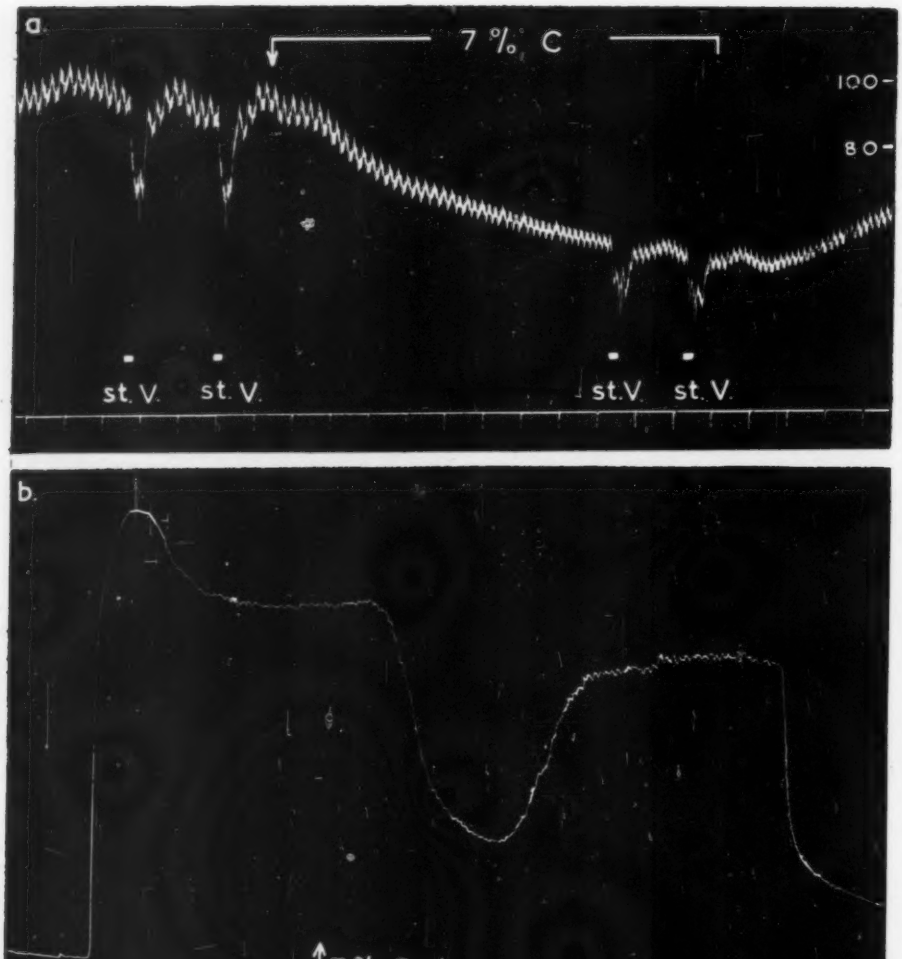

FIG. 4

(*a*) Cat blood pressure. Stimulation of vagus (st. V) was effective both before and during the administration of 7 per cent compound C.
(*b*) Cat nictitating membrane, showing sustained contraction of membrane during stimulation of preganglionic sympathetic fibres. Note relaxation of the membrane during administration of 7 per cent compound C, and subsequent renewed contraction.

TABLE IV
Effect of Compound C and Halothane on systemic output in the heart-lung preparation.

Anaesthetic	Output (ml/15 sec) Control before	Control after	During anaesthetic	Time of administration min	Output reduced to %
4% C	228	228	174	7	76
1.5% Halothane	228	228	176	7	77
4% C	228	218	170	7	74
7% C	218	222	110	5	50
2% Halothane	222	206	74	5	33

two depressant substances, and since the halothane was given after compound C it appeared to have a greater effect. Our observations, taken together, indicated that halothane had three times the depressant action of compound C. However, halothane had more than three times the anaesthetic potency of compound C, and therefore in concentrations of equal anaesthetic potency, compound C had a greater depressing action on cardiac output as measured in this way than halothane.

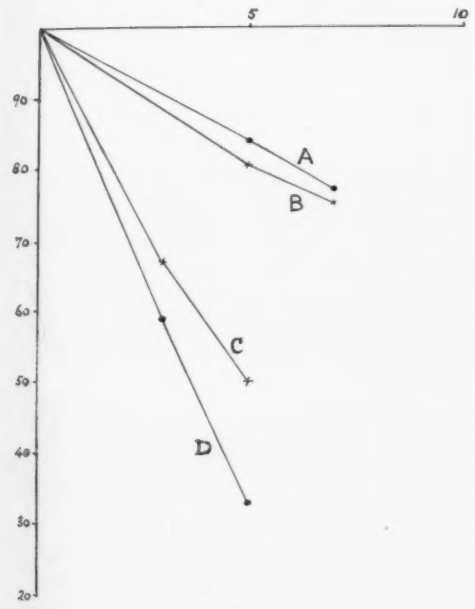

FIG. 5

Effect of compound C on cardiac output in the heart-lung preparation in comparison with the effect of halothane. Abscissa: time in min. Ordinate: output as percentage of initial output. A shows effect of 1.5 per cent halothane on output. B shows effect of 4 per cent compound C on output. Later in the experiment C shows effect of 7 per cent compound C and D shows effect of 2 per cent halothane.

Cardiac irregularities.

In the course of the observations on dogs already described, e.c.g. records were taken at intervals in 2 dogs during anaesthesia with compound C lasting 1 hour, and no irregularities were observed. We first saw periods of arrhythmia in experiments in cats which were already anaesthetized with chloralose. In one cat some arrhythmia was seen in the blood pressure record before compound C was given, at the beginning of the experiment, but this disappeared. When 4 per cent compound C was administered the blood pressure fell and an abnormality developed in which the R wave of the e.c.g. was alternately larger and smaller. This lasted for 7 min and then a normal rhythm was resumed while compound C was still being given. During the arrhythmia vagal stimulation, which was initially effective, was ineffective. When compound C was removed, the blood pressure rose and vagal stimulation again had its normal action. When, later in the experiment, 7 per cent compound C was given, the blood pressure fell and stimulation of the vagus after 4 min precipitated an arrhythmia. This stopped 1 minute after compound C was discontinued, and the blood pressure recovered.

Administration of compound C in the heart-lung preparation of a dog also caused arrhythmias. Figure 6 is an e.c.g. record in which the rhythm was normal during the administration of 4 per cent compound C, but became irregular 3 min after it was discontinued. Figure 7 is a record in which there was irregularity of the blood pressure 1.5 min after starting the administration of

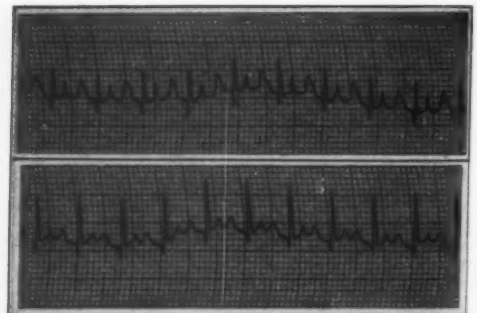

FIG. 6
E.c.g. in heart-lung preparation. The top record was taken before giving 4 per cent compound C. The middle record was taken while 4 per cent compound C was being given. The lower record was taken 3 min after discontinuance of compound C.

4 per cent compound C and again 2 min after discontinuing compound C. These irregularities were due to cardiac arrhythmia. When arrhythmias occurred they lasted only for a few minutes and ceased spontaneously. Thus in figure 7 the arrhythmia due to giving compound C lasted for 5 min and that following its discontinuance also lasted for 5 min. It is of considerable interest that arrhythmias did not recur when the same (or even a higher) concentration was administered later on during an experiment.

Histological examination of organs.

Some experiments were carried out to see whether exposure to compound C led to changes in the liver and kidney. The histological examination was very kindly made by Dr. A. H. T. Robb-Smith.

Two groups of rats were used, each rat in one group having a litter mate in the other group. The rats were from a pure bred strain supplied by the Agricultural Research Station at Compton. Their average weight was 80 grammes. One group of 5 rats was anaesthetized with 6 per cent compound C daily for 1 hour for 5 days. The second group was placed in the same apparatus daily for

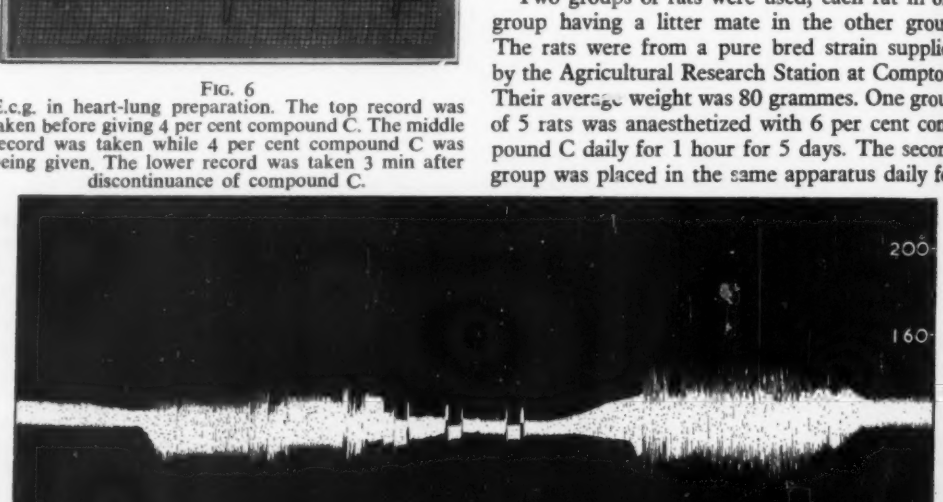

FIG. 7
Heart-lung preparation, blood pressure record. Note irregularity of record indicating arrhythmia (*a*) 1.5 min to 6.5 min after giving compound C, (*b*) 1 min to 6 min after discontinuing compound C.

1 hour for 5 days but was not anaesthetized. The rats were killed at the end of the exposure on the 5th day and the livers and kidneys were examined. The kidneys were entirely normal histologically. There was no evidence of liver cell destruction or active liver cell regeneration which are often seen in minor degrees of hepatic damage, but 2 rats showed a fair amount of fat in their Kupffer cells, and although this was to be seen to a minor extent in the control rats and in the other 3 rats treated with compound C, in these 2 rats it was rather more marked. This might be an indication of a higher fat content of the serum, possibly dietetic, but possibly associated with some change in the physical and chemical pattern of the lipoids or lipoid proteins as a result of compound C. Two of the control rats showed minor but quite definite focal regeneration of liver cells with some mitotic activity and giant liver cells which, if it had been seen in rats treated with compound C, might have indicated a minor degree of parenchymal hepatic damage.

In the second experiment there were four groups of four rats. The first group received 4 per cent compound C, the second group received 1.25 per cent halothane, the third group received 1 per cent chloroform and the fourth group were exposed in the chamber to air. Each group received the anaesthetic for 1 hour on 5 successive days. The rats were weighed during the experiment and, at the end, those receiving compound C, halothane and the controls had increased by 19 per cent; those receiving chloroform had increased only by 8 per cent. The rats were killed and paraffin sections of the liver and kidneys were stained by haematoxylin and eosin and frozen sections were stained for fat. None of the sections of kidneys of either the control or experimental animals showed any abnormality.

The liver sections of the air control series showed no abnormality. Of the animals exposed to compound C, one showed a moderate degree of mitotic activity of the liver cells and occasional binucleate forms. The three others showed a similar change but to a less degree. None of the sections showed the fatty change in the Kupffer cells observed in the earlier experiment.

In the four animals exposed to halothane, one showed mitotic activity of a similar degree to that observed in the compound C animal and another showed the slighter degree of change such as was observed in the other compound C animals. However, one of the halothane animals showed a localized but marked area of focal necrosis the interpretation of which was difficult. It might have been traumatic but equally well could have been indicative of metabolic damage. Of the four rats exposed to chloroform all showed the slighter degree of mitotic activity and all showed a quite marked fatty change both in liver cells and in Kupffer cells.

In conclusion it would seem that compound C has a mildly toxic effect on the liver, as increased mitotic activity is usually a reliable indication of some degree of metabolic damage, but this toxicity is of the same order as that of halothane, and neither substance shows the fatty changes seen when chloroform is given.

DISCUSSION

The aim of the Committee on Nonexplosive Anaesthetics is to find an anaesthetic which is nonexplosive and which is as safe in use as ether. It may be urged that halothane is not regarded as dangerous, but this opinion is probably based on the use of halothane together with a muscle relaxant, when the concentration of halothane required is low. Halothane has the great advantage for the anaesthetist that, should the effect of the relaxant be wearing off before the operation is complete, relaxation can be maintained by an increase in the concentration of halothane. It has the further advantage that muscle tone rapidly returns when halothane is discontinued. Thus the anaesthetist's task is simplified.

The picture is different, however, if halothane is to be used without a muscle relaxant and is to be given by a relatively inexperienced person as is often the case with ether. Its anaesthetic potency is high and a small increase in concentration increases the depth of anaesthesia appreciably. A weaker anaesthetic giving anaesthesia equivalent to that produced by 1.5 per cent halothane in a concentration about 5–6 per cent would be easier to handle. Compound C is such a substance, having the additional advantage that it has less depressant action on the respiration. In none of the observations on dogs was there any threat of respiratory arrest even when the concentration given was as high as 12 per cent.

Compound C is, however, an anaesthetic with a pronounced depressor action. The effect on the blood pressure was similar to that of halothane in being promptly exerted whenever compound C was given, and as promptly removed when compound C was withdrawn.

The action of compound C was tested on the output of the heart in the heart-lung preparation of the dog and compared with that of halothane. Previous observations on halothane showed that in 1.5 per cent concentration given for 10 min it reduced the cardiac output by 18 per cent (Burn, Epstein, Feigen and Paton, 1957). In the present experiments we observed that the same concentration reduced the output by (*a*) 25 per cent in 8 min, (*b*) 23 per cent in 7 min. Thus the earlier observations were confirmed. Clinical observations by Severinghaus and Cullen (1958) led them to the conclusion that 1.5 per cent halothane diminished the cardiac output by 31 per cent, but Payne, Gardiner and Verner (1959) observed no consistent change.

In the present experiments the fall in output was very slightly greater when 4 per cent compound C was given than when 1.5 per cent halothane was given. Since the anaesthetic effect of halothane in 1.5 per cent concentration was certainly greater than that of 4 per cent compound C, it follows that in concentrations of the same anaesthetic potency compound C had more depressant action on cardiac output than halothane. A contributory factor to the fall in blood pressure caused by compound C is probably a block in ganglionic transmission. It was observed that the contraction of the nictitating membrane in response to preganglionic transmission was reduced in the presence of compound C, and the onset and disappearance of the effect suggested ganglion block rather than a peripheral action on the muscle itself.

It is interesting that while halothane (except in the presence of hexamethonium) was found to have very little ganglion-blocking action on the superior cervical ganglion (Burn, Epstein, Feigen and Paton, 1957), compound C appears to have such an action.

Compound C occasionally produced cardiac arrhythmias both in dogs and in cats. These were not of long duration and they reverted spontaneously to a normal rhythm. However, in many experiments on animals with halothane, arrhythmias have not been observed, and it is therefore difficult to suggest at this stage that compound C is a sufficiently safe anaesthetic to be given a clinical trial.

The results obtained are useful in showing that halothane is one member of a class of compounds with anaesthetic properties, and that other compounds of similar structure are worth investigating in order to study the effect of changes in molecular groupings on physiological action, and also in the hope of finding the ideal nonexplosive anaesthetic.

SUMMARY

(1) The substance trifluorodichloroethane (described in the paper as compound C) is a liquid boiling at 29°–30°C which has anaesthetic properties similar to those of halothane, but has about 25–30 per cent of the potency of halothane in the dog.

(2) The induction of anaesthesia with this substance in the dog was similar to induction with halothane. This substance had less depressant action on respiration than halothane. It caused a fall of blood pressure rather greater than that caused by halothane.

(3) Compound C caused a fall of cardiac output in the heart-lung preparation similar to that caused by halothane. Four per cent of this substance had about the same effect as 1.5 per cent halothane.

(4) Compound C depressed the effect of preganglionic stimulation in causing contraction of the nictitating membrane. This effect was probably due to ganglion block.

(5) Compound C was indistinguishable from halothane in its freedom from toxic effects on the liver and kidney.

(6) But for the fact that trifluorodichloroethane caused cardiac irregularities, we would have recommended it for clinical trial. Dogs anaesthetized with this substance recovered promptly after surgical operations and were lively and well in a few hours.

ACKNOWLEDGMENTS

Our thanks are due to Professor Stacey, Professor Tatlow and Dr. Fuller for supplies of the anaesthetics studied. We also wish to thank Mr. A. J. Gunning, F.R.C.S., Dr. R. A. L. Leatherdale and Dr. J. Parkhouse, Dr. A. H. T. Robb-Smith, Mr. O. B. Saxby (for assistance in making the apparatus) and Mr. H. W. Ling (for help with the heart-lung preparations and for his care of the dogs). This work was done during the tenure by one of us (P. J. G.) of a Fellowship from the Smith, Kline and French Laboratories.

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ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

ESSAY PRIZE

The Council of the Association of Anaesthetists of Great Britain and Ireland is at present especially interested in matters which may improve the efficacy and safety of dental anaesthesia.

It has therefore been resolved to offer a prize of 200 guineas for the best essay based upon new and original work related to the subject of general anaesthesia for dental surgery. The Council would especially welcome essays dealing with the morbidity and the safe practice of general anaesthesia in the dental chair.

Essays should be submitted to the Honorary Secretary, Association of Anaesthetists of Great Britain and Ireland, 47 Lincoln's Inn Fields, London, W.C.2, on or before March 1, 1961. Intending candidates should apply to the Honorary Secretary at the above address for the regulations governing the submission of essays.

Brit. J. Anaesth. (1959), **31**, 530

LOW INCIDENCE OF "MUSCLE PAIN" AFTER SUXETHONIUM BROMIDE (BREVIDIL E)

A Comparison between Suxethonium and Suxamethonium

BY

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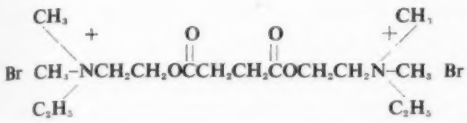
THE use of suxamethonium as a short-acting relaxant in anaesthesia is often attended by post-operative muscle pain, sometimes of great severity. Churchill-Davidson (1954) reported an incidence of 66 per cent in out-patients, two-thirds of them severe, and 14 per cent in in-patients. Hegarty (1956) found that the incidence was 20–25 per cent and that occasionally pains were so severe as to require pethidine for relief. The pains were graded in severity into (*a*) mild pains lasting 24 hours and localized to the neck and subcostal regions; (*b*) moderately severe pains affecting neck, chest and abdomen and lasting 2 days and (*c*) severe pains which were generalized, disabling and lasted 3 days. Morris and Dunn (1957) reported similarly, but an even higher figure of 72 per cent was found 5 days after discharge (22 per cent of them severe). The patients in their series all received dental treatment under general anaesthesia and were discharged within 24 hours. On the other hand these pains were said not to occur when the bromide salt rather than the chloride was used (Shegog Ruddell, 1957). However, the most recent report on a comparison between suxamethonium chloride and suxamethonium bromide again showed an incidence of 36 per cent for both compounds (Leatherdale et al., 1959). Thus most observers agree that these pains are encountered frequently and can be of considerable severity causing temporary disablement, sometimes out of all proportion to that of the operation for which the relaxant had been administered.

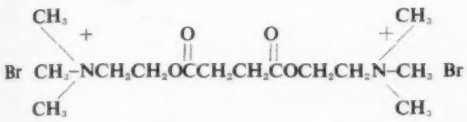
The clinical features of this condition are as follows. The onset of the pain is slow, often delayed for 12–24 hours after recovery from the anaesthetic. There is a higher incidence of the pains in females than in males and there is a considerable reduction in frequency in those patients who rest in bed after operation. The delayed onset may account for failure to recognize the incidence of pains in some patients, especially those discharged early from hospital or nursing home. Furthermore, many patients do not complain of muscle pain when the site of operation is on the upper abdomen or chest wall, because it is then thought to have been caused by the operation. Similarly pains and stiffness in the back and shoulders are often interpreted as due to the posture on a hard operating table. On the other hand, information is readily volunteered when the pains are more severe and generalized.

Although the vast majority of operations can be conducted with entire satisfaction under long-acting relaxants alone (Enderby, 1959), it cannot be denied that a powerful short-acting agent has great advantages for certain operations, especially endoscopic examination of the bronchi and larynx and for short periods of profound relaxation, as in upper abdominal surgery and for intubation. However, a short-acting drug such as suxamethonium which has such prolonged after-effects cannot be considered as truly "short-acting" and its use should be reserved for those occasions where its advantages more than compensate for such severe disadvantages. An investigation has been made of suxethonium as a replacement for suxamethonium in an attempt to find a more acceptable relaxant with similar properties.

Suxethonium bromide (Brevidil E) is a synthetic muscle relaxant of the depolarizing type with a very brief duration of action, and this is supplied as the bromide. Its formula is



and compares with suxamethonium which is



This very slight difference results in the human in a weaker and slightly shorter action than that of suxamethonium (Foldes et al., 1956).

CLINICAL INVESTIGATION

The incidence of muscle pain with suxethonium has been carefully investigated and compared as accurately as possible with suxamethonium when used in the same way. The majority of the operations were maxillo-facial and plastic and they were mostly performed by one surgeon. Suxamethonium was administered to one group and suxethonium to the other. All patients were then watched closely for complaints of pain during the two days immediately after operation. In each case questions were asked only about their general health and comfort, without enquiring specifically about the neck, shoulders, chest, etc. Females comprised 86 per cent of the patients in both groups, all of whom were treated as in-patients for 4–7 days after operation. With few exceptions all were instructed to remain in bed for 24 hours postoperatively. All these anaesthetics were administered personally by the writer, thus enabling a more exact comparison to be made. Each patient was induced with thiopentone and decamethonium and to this was added 50 mg of suxamethonium chloride or 50 mg (cation) of suxethonium before intubation. Both drugs enhanced slightly the relaxation of decamethonium for intubation, but no individual difference was observed in their actions. The operations were performed under nitrous oxide with further doses of thiopentone and decamethonium if required, and some patients were given a small concentration of halothane. Most operations were conducted under controlled hypotension. No further injection of suxamethonium or suxethonium was made during the course of the operation except on rare occasions to assist relaxation and then usually for operations within the abdomen, but such instances were few in number.

RESULTS

A careful postoperative investigation of these patients showed that those receiving suxamethonium exhibited pain in 17 per cent (10 patients in a total of 60) and 2 of these were moderately severe. Those receiving suxethonium exhibited pain in 4.2 per cent (12 patients in a total of 285) and 11 of these were slight or very slight, and 1 was moderately severe. This investigation started with suxethonium and after it had been administered to 160 patients successively a change was made to suxamethonium with the intention of performing at least 100 similar administrations for comparison. The frequency of pain with the latter was such, however, that after 60 administrations this trial was abandoned as it was not considered justified to continue further.

A FURTHER TRIAL

Another comparison was also made in which 25 mg of suxamethonium was given to one group of 22 patients and 75 mg of suxethonium to another group of 50 patients, thus comparing approximately equipotent doses. In this trial *every patient was asked specifically* about pains or stiffness in the neck, shoulders, back and upper abdomen on each of the two days immediately after operation. By this means so many of the "personal factors" affecting these figures were avoided, and quite different results were obtained. Thus 50 per cent of those receiving suxamethonium had pains and stiffness within the first two days, whilst 34 per cent of those receiving suxethonium exhibited similar findings. These figures do not at first appear to bear much relationship to those already presented, but it was also found that 18 per cent (4 patients) of those receiving suxamethonium complained spontaneously of these pains (i.e. before questioning) (although in every case they were classified as only "slight" or "v. slight") whilst only 2 per cent (1 patient) of those receiving suxethonium complained likewise. These results are therefore in keeping with those previously reported and

serve to stress the necessity for careful questioning when assessing the incidence of pain after these drugs. They also show that with suxethonium there is an overall reduction in the incidence of these pains, and most important of all that these pains are usually so mild that no complaint is made by a very high percentage of patients. On the other hand, with suxamethonium pains are more frequent and severe and complaints are encountered more often.

One further comparison proved possible during this investigation. One patient (male) was anaesthetized with the assistance of suxamethonium (90 mg) for relaxation and at a subsequent operation with suxethonium (200 mg). He volunteered the information afterwards that the second administration was "infinitely more comfortable" than the first. After the first operation he had suffered considerable muscle pains for 24–36 hours, whilst after the second operation he was pain-free. More recently he has had two further anaesthetics, in both of which suxethonium was used and after both he was pain-free.

These results all suggest that suxethonium has the definite advantage of a considerable reduction in postoperative muscle pain. On the other hand, the relaxation it provides is different from that of suxamethonium for it is of shorter duration and larger doses may have to be employed to give an equivalent effect. This difference is apparent during bronchoscopy, but it is slight and does not interfere with the successful performance of the operation, nor is it a disadvantage in other surgical operations. Indeed in the routine indications for the use of a short-acting relaxant this drug is satisfactory and the small difference in its action from suxamethonium does not detract from its usefulness. It is indeed a great advance in short acting relaxants, for it helps to maintain the postoperative comfort, and well-being of the patient whilst achieving a satisfactory relaxation for the anaesthetist and surgeon.

SUMMARY

A comparison has been made between suxamethonium and suxethonium as to the incidence of postoperative muscle pain.

Spontaneous complaints of pain occurred in 17 per cent of 60 patients receiving suxamethonium, and in 4.2 per cent of 285 patients receiving suxethonium.

Direct questioning indicated an incidence of 50 per cent in 22 patients receiving suxamethonium and 34 per cent in 50 patients receiving suxethonium. In this comparison spontaneous complaints occurred in the ratio of 18 per cent for suxamethonium to 2 per cent for suxethonium.

There is a considerable overall reduction in the incidence and severity of pain with suxethonium.

ACKNOWLEDGMENT

My thanks are due to May & Baker for supplies of Suxethonium Bromide (Brevidil E). This compound is now available as a solution containing 150 mg per ml.

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BUTHALITONE SODIUM

Its effect on the foetus and its rate of passage across the human placenta

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INTRODUCTION

The prime object of obstetric anaesthesia is to maintain an adequate state of analgesia and narcosis of the mother while the foetus remains unaffected. With this object in view, the following thirty-four cases of Caesarean section and forceps delivery were anaesthetized by a combination of a thiobarbiturate induction, followed by the nitrous oxide, oxygen and muscle relaxant sequence.

The brevity of action, and the minimal respiratory depression which some workers have attributed to buthalitone sodium (Weese and Koss, 1954; Bergentz and Arosenius, 1955) are points in favour of the use of this drug as a means of induction of anaesthesia for obstetric procedures, even compared with thiopentone sodium.

Crawford and Kane (1956) showed that the placenta offered no significant barrier to thiopentone sodium. Moreover, the cord plasma level of thiopentone sodium decreased as time between induction and delivery increased. Hence, there was no reason to limit the use of thiopentone sodium to those obstetric cases in which a rapid delivery was to be expected—the "12-minute rule" of Hellman and co-workers (1944).

The agents used for maintenance of anaesthesia would not be expected to cause any central depression of the foetus. Suxamethonium chloride was used throughout as a muscle relaxant.

EXPERIMENTAL METHODS

(a) *Clinical*

All patients in this series were premedicated with atropine sulphate 0.6 mg either subcutaneously or intramuscularly, depending on the urgency of the procedure. In addition, those patients who had eaten or drunk recently were given apomorphine 1.5 mg intravenously to induce vomiting (Holmes, 1956).

Owing to the obvious difficulties of a weight/dose calculation, the majority of cases being emergencies, a fixed dose of buthalitone sodium was used for induction. Five hundred mg were rapidly injected as a 10 per cent solution through a Gordh needle placed in a vein on the dorsum of the left hand, and this was followed by 100 mg of suxamethonium through the same needle. The patient's lungs were then inflated with oxygen and intubated with a cuffed endotracheal tube under direct vision, the tube being well lubricated with analgesic paste. When this stage was reached the surgeon was allowed to proceed.

Anaesthesia was maintained with nitrous oxide and oxygen in a ratio of 3:2 using a Waters canister for carbon dioxide absorption. Those cases which had previously been given trichloroethylene for analgesia were given nitrous oxide (6.1 l./min) and oxygen (4.1 l./min), the absorber being removed from the circuit. Intermittent doses of suxamethonium, 25 mg, were given as needed, and respiration was controlled.

As the patient was already receiving a 40 per cent oxygen mixture, no attempt was made to inflate the lungs with pure oxygen prior to delivery of the foetus. After delivery of the baby the patient was given papaveretum 22 mg or pethidine 50 mg intravenously, and maintained as before. At the completion of the procedure,

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pharyngeal toilet was performed under direct vision before extubation. Papaveretum was used as the postoperative sedative.

Cord and maternal blood samples were taken simultaneously just after delivery. The cord sample was taken from the umbilical vein using a syringe with a wide-bore needle, approximately 10 ml of blood being withdrawn. The maternal sample (10 ml of blood) was taken from a vein in the dorsum of the right hand at the same time as a foetal sample was being obtained. The following data were also recorded:

(1) Time taken in minutes from induction of anaesthesia to delivery.
(2) The time in minutes from the umbilical cord being clamped until the first cry or the onset of spontaneous respiration.
(3) The tone and colour of the foetus on delivery.
(4) Intermittent recordings of pulse and blood pressure throughout the operation.

(b) *Laboratory*

The blood samples were transferred to oxalated tubes and the red cells spun off in a centrifuge. The plasma was analyzed for buthalitone sodium content by the method developed by Crawford and Kane (1956) for thiopentone sodium. The validity of this method when applied to buthalitone sodium was checked by the addition of known amounts of buthalitone sodium to samples of maternal and cord plasma from patients not receiving barbiturates and analysis of the samples. The reproducibility was of the order ± 10 per cent, which was taken as the limit of possible error. Kane and Smith (1959) have shown that this method of estimation does not lead to errors caused by metabolic products of buthalitone sodium.

RESULTS

Clinical and laboratory results are given in table I. Laboratory results are also given in figures 1 and 2.

There were no maternal or infantile deaths in the series, and postoperative convalescence was uneventful in all cases, no respiratory or anaesthetic complications being recorded. All the babies on delivery had a normal tone, and their colour was good. From the table it will be noted that resuscitation required was minimal, only two babies requiring endotracheal intubation and artificial respiration for a short period before adequate spontaneous respiration was established. Recovery of the mother was rapid; in many instances the patient was able to move off the table unaided and appeared quite comfortable. There was no undue incidence of postoperative vomiting.

Figure 1 shows the relationship between maternal and cord plasma concentrations of buthalitone at the time of delivery. Although the scatter of data is much greater than that of Crawford and Kane (1956) for thiopentone sodium, a difference between the behaviour of the two drugs is at once apparent. In the case of thiopentone sodium, the maternal and cord concentrations were equal, the placenta apparently offering no barrier to the passage of thiopentone sodium. This was clear from their figure corresponding to our figure 1. The overwhelming majority of their data fell within the estimated limits of error to the 45° line. In the case of buthalitone sodium, although

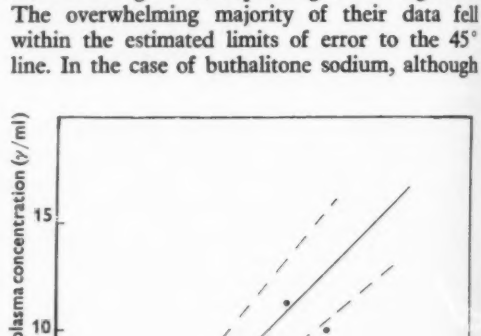

FIG. 1

Relationship between maternal and cord buthalitone sodium plasma level at time of delivery.

——— Curve of maternal level=Cord level.

- - - Estimated limits of experimental error to this curve (±10 per cent possible error to each result).

TABLE I

Clinical and laboratory data for buthalitone sodium in obstetric procedures.

TABLE I

Clinical and laboratory data for buthalitone sodium in obstetric procedures.

Case no.	Maternal weight (kg)	Dose of buthalitone (mg)	Dose (mg/kg)	Foetal B.W. (kg)	Time from induction to delivery (min)	Maternal concn. (γ/ml)	Cord concn. (γ/ml)	Time from delivery to first cry (min)	Resuscitation	Procedure and indication
1	—	500	—	3.32	11	7.9	7.9	0	Nil	L.S.C.S.
2	67.0	500	7.46	3.95	7	10.0	9.7	0	Nil	F.D., foetal distress.
3	60.0	500	8,33	3.58	7½	12.6	6.6	½	Nil	Elective L.S.C.S., previous C.S., disproportion.
4	64.8	500	7.72	3.40	10	11.0	11.4	0	Nil	Elective L.S.C.S., long labour in first pregancy followed by foetal death.
5	80.9	400	4.94	4.29	11	4.6	1.0	½	Nil	L.S.C.S., uterine inertia, previous C.S.
6	57.3	500	8.73	2.72	20	6.7	3.4	0	Nil	L.S.C.S., toxaemia, placenta praevia, previous C.S.
7	50.9	500	9.82	2.61	20	7.4	8.3	0	Nil	L.S.C.S., placenta praevia, A.P.H. at 36/52.
8	—	500	—	3.83	25	4.2	5.1	1½	Nil	F.D., uterine inertia, post maturity.
9	82.3	500	7.07	4.00	19	4.7	0.3	0	Nil	L.S.C.S., post maturity, foetal distress, maternal distress, uterine inertia.
10	66.6	500	7.51	3.66	23	16.2	3.9	½	Nasal O_2	L.S.C.S., malpresentation, previous C.S.
11	68.6	500	7.29	2.33	16	5.1	4.5	0	Lobeline 3 mg	L.S.C.S., placenta praevia, A.P.H. at 36/52.
12	62.9	500	7.95	2.93	12	11.5	9.2	½	Nil	Elective L.S.C.S., contracted pelvis, previous C.S.
13	51.8	500	9.65	3.86	15	7.3	5.6	1	Nil	Elective L.S.C.S., malpresentation, pelvis contraction.
14	64.5	500	7.75	3.81	8	8.6	2.6	1½	O_2 through mask	L.S.C.S., three previous pregnancies F.D., S.B., and C.S.
15	77.7	500	6.43	4.55	15	8.3	4.3	2	O_2 through mask	L.S.C.S., failed trial of labour.
16	82.7	500	6.05	4.74	9	3.9	3.2	0	Nil	Elective L.S.C.S., eldery primigravida, post maturity, uterine inertia.
17	85.2	500	5.87	3.29	8	11.0	0.6	½	Nil	L.S.C.S., A.P.H. at 36/52, previous S.B.
18	—	400	—	3.27	5	8.7	7.0	½	O_2 through mask	L.S.C.S., foetal distress, uterine inertia.
19	56.8	500	8.81	4.16	7	6.1	4.1	½	O_2 through mask	L.S.C.S., uterine inertia, malpresentation.
20	—	500	—	3.69	5	11.0	3.9	0	Nil	Elective L.S.C.S., unstable presentation, previous C.S.
21	71.5	500	6.99	3.81	11	6.9	4.9	½	O_2 through mask	F.D., contracted pelvis, malpresentation.
22	61.6	500	8.12	3.68	11	14.2	6.5	½	Nil	Elective L.S.C.S., previous C.S.
23	68.2	500	7.33	4.43	5	4.4	4.2	½	Nil	L.S.C.S., contracted pelvis, previous C.S.
24	82.3	500	6.07	3.86	5	10.9	6.5	¾	O_2 through mask	L.S.C.S. and sterilization, para-12, scarred cervix.
25	75.7	400	5.28	3.13	7	6.2	3.6	1	O_2 through mask	L.S.C.S., maternal distress, uterine inertia.
26	60.2	500	8.31	2.54	8	8.6	0.1	½	Nil	L.S.C.S., foetal distress, elderly primigravida.
27	—	500	—	1.76	5½	8.7	3.2	2	Endotracheal O_2	L.S.C.S., toxaemia.
28	86.6	500	5.77	2.30	31	3.9	3.9	½	O_2 through mask Lobeline 3 mg	L.S.C.S., subtotal hysterectomy, para-5, pre-eclamptic toxaemia, essential hypertension.
29	69.3	500	7.21	3.35	12	10.6	8.2	0	Nil	E.U.A., L.S.C.S., placenta praevia.
30	88.1	500	5.67	3.52	12	9.0	6.2	½	O_2 through mask	L.S.C.S., foetal distress, hypertension.
31	52.3	450	8.60	2.66	10	12.9	10.1	1	Endotracheal O_2	Elective L.S.C.S., previous C.S.
32	81.4	500	6.14	2.70 2.19	9 13	7.0	5.0 4.6	0 2	O_2 through mask	L.S.C.S. and sterilization, twin pregnancy, toxaemia, two previous C.S., abnormal pelvis.
33	80.7	500	6.19	2.81	21	5.4	4.6	0	Nil	E.U.A., L.S.C.S., central placenta praevia.
34	74.1	450	6.07	3.13	15	5.9	3.6	0	Nasal O_2	L.S.C.S., contracted pelvis, breech presentation.

L.S.C.S. = Lower segment Caesarean section
F.D. = Forceps delivery
C.S. = Caesarean section
A.P.H. = Antepartum haemorrhage
S.B. = Stillbirth
E.U.A. = Examination under anaesthesia

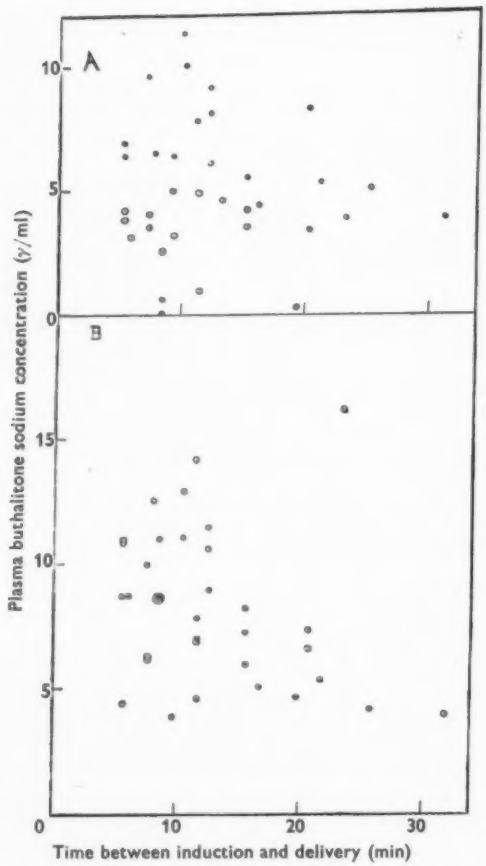

FIG. 2

Relationship between plasma buthalitone sodium level and duration of operation.

A Cord level. B Maternal level.

considerable quantities of the drug reach the foetus, there is a distinct tendency for the cord plasma concentration to be lower than that of maternal plasma. The data of figure 1 are not sufficiently conclusive to decide whether there is a time delay before buthalitone sodium begins to appear in the foetal circulation or whether there is a simple concentration gradient across the placenta. Figure 2 shows the variation of plasma concentration of buthalitone sodium at time of delivery with the length of time between induction of anaesthesia and delivery, both for the mother and the cord. Here again there is a difference of behaviour between buthalitone sodium and thiopentone sodium. Crawford and Kane (1956) found that the cord plasma concentration of thiopentone sodium decreased as the time between induction and delivery increased. The data of figure 2 were too scattered to allow any definite trend to be discovered. The scatter of data in figure 2A may, in part, be attributed to variability of the placental barrier. There was, however, no indication that cord plasma level increased with time.

DISCUSSION

The clinical results show that buthalitone sodium is in every way a satisfactory drug for induction of anaesthesia in obstetric procedures. The condition of the baby at birth was, in the main, excellent and there was no evidence of respiratory depression.

An attempt by Kane and Smith (1959) to obtain a correlation between plasma concentrations of buthalitone sodium and stages of recovery from anaesthesia failed to reveal any correlation. Hence the data on foetal plasma concentrations of buthalitone sodium reported here should not be isolated from the clinical findings, and can only reveal movement of the drug from mother to foetus without giving any information concerning possible depressant effects of the drug.

The data on cord plasma concentrations, whilst not as clear-cut as those for thiopentone sodium (Crawford and Kane, 1956), nevertheless indicate that a smaller proportion of thiobarbiturate reaches the foetus when buthalitone sodium is used than in the case of thiopentone sodium. The placenta, therefore, offers a partial barrier to the passage of buthalitone sodium. As in the case of thiopentone sodium, however, there is no evidence that rapid delivery of the baby is a prerequisite to the use of buthalitone sodium.

SUMMARY

Maternal and cord buthalitone sodium plasma concentrations at time of delivery are reported for thirty-four obstetric patients in whom anaesthesia was induced by buthalitone sodium. Time intervals between induction and delivery are also reported. The cord plasma concentration tended

to be significantly lower than that of the maternal plasma, but the variation from patient to patient was too great to permit any definite conclusions to be drawn regarding the mechanism of retardation to passage across the placenta. There was no evidence that the cord concentration increased as the time between induction and delivery increased. Clinically, the response of mother and baby to buthalitone sodium induction was excellent.

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PUDENDAL BLOCK ANAESTHESIA IN OBSTETRICS

A Review of 510 Operative Deliveries

BY

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THE mitigation of pain in childbirth has always been the anxious concern of obstetricians. Since Simpson administered the first obstetrical anaesthetic in 1847, this subject has been controversial, and an ideal solution has yet to be found. In recent years, the rise in popularity of anaesthesia in childbirth has, in spite of improved techniques, brought with it greater risks to mother and baby. Hingson and Hellman (1956) consider maternal deaths resulting from or relating to anaesthesia to be fifth in importance, while Nesbitt (1957) states that one eighth of all maternal deaths are due to such causes; most of these are preventable.

According to statistics in New York City (Hellman and Hingson, 1952), 155 of 330 maternal anaesthetic deaths resulted from aspiration of vomit during or immediately after anaesthesia. No precise figures have been given for foetal mortality. Lister and Buchanan (1957) found a considerably lower incidence of neonatal asphyxia in babies without foetal distress, delivered by forceps under pudendal block, as compared with those delivered by forceps under general anaesthesia.

The selection of the method of anaesthesia is not easy. While the chief danger in inhalational anaesthesia is aspiration resulting in pneumonitis, spinal and caudal anaesthesia require the presence of a skilled anaesthetist and carry a risk of circulatory collapse and various neurological complications. According to Eastman (1956), Hingson reported 43 maternal deaths in the course of 200,000 administrations of continuous caudal analgesia, and Halperin and Levine (1952) had 5 maternal deaths in a total of 21,617 conduction anaesthesias in obstetrics.

Most authors, however, agree that the safest and most nearly ideal anaesthesia for delivery is provided by pudendal nerve block. This was first described by Mueller in 1908, while Ilmer (1910) and Kurz (1916) used it with good results. Since then the method has been practised and recommended by many obstetricians, and a great number of reports have appeared in the literature advocating its usefulness, simplicity and safety. Greenhill (1947) has repeatedly entered strong pleas in favour of local anaesthesia in obstetrics; yet it has failed to gain the popularity it deserves.

The advantages of pudendal nerve block for childbirth are numerous; its drawbacks are few. No special skill or knowledge is required and the obstetrician is independent of the skilled anaesthetist. By using pudendal block pain relief is attained without general or local complications, with only rare side-effects in the parturient, without interference with the process of labour itself or with the action of the uterus, and without danger to the mother or to the child.

It is especially indicated in prematurity and in patients who have pulmonary or cardiac complications, and in those pregnancies complicated by pre-eclampsia or diabetes. This block is valuable in cases of breech presentation, where anaesthesia of the perineum alone permits the voluntary bearing-down efforts of the parturient, thus greatly facilitating delivery. In twins, delivery of the second baby may be undertaken at leisure and without fear of the effect of the anaesthetic upon it. Pudendal block is satisfactory for spontaneous deliveries, low forceps and easy mid forceps, and in assisted breech deliveries. It has few limitations. Not all women are suitable candidates. It should not be attempted in high-strung or unco-operative parturients. Obstetrical operative procedures that require complete relaxation of the uterus, such as internal podalic version and breech extraction or

difficult mid-forceps extractions, should not be attempted with this type of anaesthesia.

Recently, the use of hyaluronidase, a mucolytic enzyme, in conjunction with the anaesthetic solution has been reported (Douglas and Vosburgh, 1951; Heins, 1951; Hibbard and Grassie, 1955; Britton, 1953; Moore, 1950; de Alvarez and Gray, 1954). It is a safe, nontoxic, simple agent for increasing the efficiency of pudendal block in obstetrics. In an extensive study Moore (1950) came to the conclusion that hyaluronidase enhances the penetration of desired substances by increasing the rate of diffusion and absorption by neutralizing the hyaluronic acid in the interstitial spaces of the tissue. Thus the mixed anaesthetic solution does not necessarily have to be deposited on the nerve in order to be effective, and this facilitates the technique of administration considerably. Also, it accelerates the onset of anaesthesia.

Various techniques of pudendal nerve block have been described. The most common method, and the one we use, is the transperineal, which has been used in large series of cases by many obstetricians (Dugger, 1956; Scott and Gadd, 1957; Woolsey, 1955; de Alvarez and Gray, 1954; Douglas and Vosburgh, 1951; Harris, 1954). More recently the transvaginal technique has been highly recommended by several authors (Kobak, 1956; Wilds, 1956; Lee, 1959; Huntingford, 1959).

MATERIALS AND METHODS

Our series consists of 510 patients who were delivered operatively of 525 babies in the obstetrical department of the Beilinson Hospital between 1955 and 1959.

Their ages ranged from 18 to 41 years; 342, or 67 per cent, were primiparas, and 168, or 33 per cent, were multiparas. Table I lists the complications of pregnancy and labour in which a pudendal block was performed. Parturients with cardiac disease include 9 after commissurotomy, in 2 of whom cardiac decompensation occurred in labour. In the group with pulmonary disease, 12 patients had undergone lobectomy or pneumonectomy for pulmonary tuberculosis.

The parturients were carried through labour on an intravenous analgesic "cocktail" of pethidine-promethazine-levallorphan (Eckerling, Goldman and Gans, 1959), or on intramuscular pethidine alone. Thus, at the time the parturients were ready for delivery, many of them were quite relaxed and drowsy, sleeping during intervals and waking slightly during contractions. The procedure was explained to those who were awake, emphasizing the fact that they would be free of pain of perineal stretching during delivery, while uterine contractions would not be affected, but would be felt as before.

TABLE I

Complications of pregnancy and labour in which pudendal block was used.

Complications	No. of patients
Cardiac disease	34
Pulmonary disease	38
Diabetes	12
Toxaemia of pregnancy	28
Severe myopia	9
Blood dyscrasia	17
After thyroidectomy	6
After nephrectomy	4
After previous Caesarean section	19
Premature delivery	32
Prolonged labour	65
Foetal distress	61
Deep transverse arrest	7
Persistent occiput posterior	12
Total	344

A mixture of 1 per cent lignocaine (Esracaine brand) with hyaluronidase (Hyalase) 1,500 I.U. and 0.5 ml of adrenaline 1:1000 was used to produce anaesthesia in form of a pudendal nerve block. Approximately 50 ml of this solution were injected in the following manner:

TECHNIQUE

A 10-ml Luer-Lok syringe with a 6-inch 18-gauge spinal needle is used. A weal is made in the skin on each side and the needle is introduced at about midway between the anus and the ischial tuberosity. Two fingers in the vagina locate the ischial spine and the course of the needle is guided towards it. Approximately 10 ml of the anaesthetic solution are deposited near the inferior aspect of the ischial spine and around it, in order to anaesthetize the pudendal nerve as it enters Alcock's canal alongside the pudendal vessels. (It has been advocated that some blood be aspirated from the pudendal blood vessels, in order to be certain that one is in Alcock's canal. We did not

find this procedure essential, since the use of hyaluronidase seems to provide enough diffusion of the lignocaine.) The needle is withdrawn and 5 ml are injected under the skin along the inner aspect of the labium majus, to include branches from the ilio-inguinal nerve. Five ml of the mixture are injected near the tuberosity, where branches from the posterior femoral cutaneous nerve pass. Finally, the perineum in the region of the fourchette and the episiotomy site are infiltrated with another 5 ml.

The same procedure is repeated on the other side. The plunger of the syringe is withdrawn each time before injection, in order to avoid accidental injection of the solution into a blood vessel. The whole procedure takes approximately 5 minutes.

The block was usually given in the primipara at full dilatation with the head below the ischial spines; in the multipara it was administered earlier, as soon as a rim of cervix was left.

RESULTS

Results were graded as excellent in those cases in which the operative procedure was completed without pain or discomfort to the patient. They were deemed satisfactory when a slight amount of discomfort was experienced by the patient, and poor when the pudendal block had to be supplemented with another type of anaesthesia.

Table II indicates the degree of anaesthesia achieved. It was excellent in 95 per cent of cases and satisfactory in 3 per cent. In 6 deliveries general anaesthesia with ether was used to supplement the block. In one such case difficult mid-forceps rotation and in another internal podalic version and extraction had to be performed. The remaining 4 patients were, on re-evaluation, considered unsuitable to this type of anaesthesia, being apprehensive and unco-operative.

TABLE II

Degree of anaesthesia achieved with pudendal block.

Degree	No. of patients	Per cent
Excellent	485	95
Satisfactory	15	3
Poor	10	2
Total	510	100

Pudendal block was used to produce anaesthesia in low forceps, a limited number of mid-forceps deliveries, and in breech deliveries. In table III, the method of delivery in our 510 patients is listed. It is worth noting that this method was successful in almost 100 per cent of low forceps deliveries.

TABLE III

Type of delivery in which pudendal block was used.

Method	Number of babies delivered
Low forceps	460
Mid forceps	14
Assisted breech delivery	39
Breech extraction	12
Total	525

The onset of complete perineal anaesthesia occurred approximately 3–4 minutes after the infiltration was completed, although many were anaesthetic immediately. It was usually effective for an average period of 1 hour; consequently it was very rarely necessary to infiltrate the episiotomy site with additional lignocaine for the repair.

During and after injection of the anaesthetic mixture neither pulse rate nor blood pressure nor respiratory rate was altered. No significant increase in postpartum bleeding was noted; it seemed too that secondary uterine inertia and uterine atony were rare. There were no local infections or oedema and only one minor haematoma of the perineum was found, which, however, did not impair healing of the episiotomy. No other side-effects or complications occurred; however, in one case which has previously been reported (Goldman, 1958) a short psychotic reaction supervened, most probably due to an overdosage of lignocaine. No maternal deaths occurred in this group.

Of the 525 babies, there were 7 foetal deaths. Two babies born with multiple congenital malformations died several days after delivery. Another baby died of erythroblastosis foetalis. Four more infants born prematurely and weighing less than 1.5 kg died 1 to 5 weeks after delivery.

Five infants delivered by low forceps because of foetal distress were born with mild or moderate

asphyxia and required resuscitation. All recovered ultimately.

No foetal death or asphyxia was considered due to anaesthesia.

COMMENT

Today more than ever before women desire alleviation of pain in labour and delivery. This desire should not be denied. It has been said that it is no triumph of obstetric art to deliver a woman safely but to leave her mind so full of vivid and unhappy memories that she refuses to face childbed again! Nevertheless, though painless childbirth presents a definite advantage to the parturient, there are dangers associated with each method of anaesthesia. Considering the voluminous literature on pain relief, it is quite evident that the ideal anaesthetic method for delivery has not yet been found. Pudendal block anaesthesia seems to have achieved a great degree of safety to mother and baby, while contributing to the comfort of the parturient and relieving her agony in childbirth.

Our series included 510 operative vaginal deliveries in whom the pudendal block method provided satisfactory anaesthesia for delivery in at least 98 per cent of parturients, without jeopardizing the safety of either the infants or the mothers. Almost no side effects occurred and postpartum haemorrhage seemed to be decreased with this method.

In view of its safety and adequacy it is difficult to understand why the popularity of this method has been limited. One limitation is that the perineal reflex and the resultant urge to bear down are lost; the patient therefore has to be instructed to bear down. When dealing with spontaneous or assisted breech deliveries this may possibly be of importance, though uterine contractions are not affected; however, when forceps extraction is planned, this fact seems no disadvantage.

Several other objections have been advanced (Taylor and Jack, 1949), including the time interval, special skill required in performing the block, incomplete relief, failure of relaxation of the uterus, oedema at the site of injection, and others. It appears that most of these limitations have been overcome by the addition of hyaluronidase and adrenaline to the lignocaine solution. The undesirable shortening of anaesthesia caused by hyaluronidase is eliminated by the addition of adrenaline, which increases the duration of anaesthesia, permitting early administration of the anaesthetic solution.

In conclusion, although no anaesthesia for parturition is ideal, it is believed that pudendal nerve block has the largest number of advantages. In conjunction with adequate sedation in labour it should be considered the simplest and safest method in most obstetrical cases.

SUMMARY

A survey of 510 operative vaginal deliveries under pudendal block anaesthesia with a mixture of lignocaine, hyaluronidase and adrenaline has been presented. The safety to mother and newborn with this method of anaesthesia as compared with other methods, has been evaluated. The special value of pudendal nerve block in deliveries complicated by maternal disease has been emphasized. Satisfactory pain-relief in delivery was obtained in approximately 98 per cent of cases.

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The Faculty of Anaesthetists of the Royal College of Surgeons of England are proposing to hold a course in the measurement of cardio-respiratory function during anaesthesia and surgery, in the week commencing February 22, 1960. It is proposed that the course shall last 5½ days, and will be composed of lectures, demonstrations, and practical work. It is clear that membership of the course will be limited and the proposed number is 15. Enquiries and applications for membership for the course should be made to Professor Ronald Woolmer, Faculty of Anaesthetists, Royal College of Surgeons of England, before January 18, 1960.

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THE SUPPLEMENTATION OF REGIONAL ANALGESIA

BY

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IN the early literature on local analgesia no mention is made of sedation of the patient during surgery. Indeed, it was even recommended that a stimulant be given just before the injection of local anaesthetic "to help in preventing an undue amount of shock" (Probyn-Williams, 1901). In 1899 Ceci described his use of morphine injected a few minutes before operations carried out after infiltration with a solution of cocaine. Metzenbaum, in 1900, initiated the use of a combination of morphine and scopolamine to sedate patients operated on under local analgesia and this combination was later reported on by Lewis (1923). In the early part of this century there developed a technique which employed these two drugs by repeated injections. Thus Penkert (1906) used 11 mg morphine and 0.32 mg scopolamine 2½ to 3 hours pre-operatively and repeated this 1 hour later. He stated that the patients arrived in the operating room as if under chloroform narcosis and had no recollection afterwards. Brenitzer (1915) recommended three injections starting 1½ hours pre-operatively. This multiple dose technique was, however, rejected by Labat (1923) who believed that a second dose often acted as an excitant rather than a sedative and he preferred a single dose for premedication except in very nervous patients.

Papaveretum, which was introduced into anaesthesia by Schneiderlin in 1900, was employed together with scopolamine by Gray (1911) to supplement regional analgesia. A similar technique was being widely employed in Germany at this time (Stenglein, 1912; Colmers, 1912; Diwawin, 1912).

In the years that followed various opiates had their advocates, morphine, dihydromorphinone (Dilaudid) (Rost, 1933; Biot, 1934; Siebner, 1935; Betlach, 1941) and papaveretum being the most favoured drugs, and even codeine phosphate was found useful by some (Tomlin, 1923; Moersch, 1942).

More recently desomorphine (Schurch, 1945), ketobemidone (Lorenzini, 1950; Ferrero, 1951), pethidine (Hori and Gold, 1944) and alphaprodine (Weiner, 1955) have been used for this purpose.

The next development was the administration of a medium acting barbiturate in addition to the opiate and belladonna preparation (Axelrod, 1934; Mason, 1937). The barbiturate was administered 1 hour or more before the narcotic to avoid delayed absorption from the pylorospasm caused by the opiate. The barbiturate, in addition to increasing the sedation, had the advantage of reducing the risk of toxic reactions to the local anaesthetic agent. Such a combination of drugs is still widely employed.

Tribromethanol (Avertin) had a brief spell of popularity for supplementing local analgesia (De Takats, 1931; Featherstone, 1934; Boyd, 1935; and Report of Council on Pharmacy and Chemistry, 1937) but fell out of favour because of toxic effects (Beecher, 1938). Rectal paraldehyde together with hypodermic papaveretum (Graves, 1937) and magnesium sulphate together with morphine (King, 1923) also enjoyed transient favour.

In the third decade of this century the intravenous route for the administration of supplementing narcotics received considerable attention. Thus Kirschner (1935) advocated intravenous morphine-scopolamine supplementation and this route was employed by Siebner (1935) with dihydromorphinone-hyoscine. Bloch and his colleagues (1936) proposed the intravenous injection of morphine and hyoscine together with

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narcotine and ephedrine as "corrective agents." The use of intravenous morphine by slow injection was recommended if the patient was insufficiently sedated during operations under local analgesia or if the effect of the block was wearing off (Sebrechts, 1934; Betlach, 1937). Intravenous morphine was also recommended by Presman and Schotz (1943) for the patient who arrived in the anaesthetic room insufficiently sedated.

The difficulties associated with the parenteral use of sedatives led some, at an early date, to supplement local analgesia with light nitrous oxide-oxygen anaesthesia (Hewer, 1920; Crile, 1925) and this method is used by many anaesthetists today. Others have supplemented regional blocks with thiopentone, either alone or with nitrous oxide and oxygen (Evans, 1949) and even with potent gaseous anaesthetics (Saklad, 1936).

The introduction of the narcotic antagonists offered the possibility of avoidance of the respiratory depressant effects of the narcotics and combinations of narcotic analgesics with antagonists have been employed with some success to supplement regional analgesia (Stoelting and Hicks, 1956; Lipson and Bradford, 1957).

The advent of the tranquillizing drugs suggested a new and possibly advantageous approach to the problem.

PRESENT STUDY

For the present purpose a few phenothiazine derivatives appeared to be worthy of trial and of these promazine (Sparine) (see figure 1) was chosen because it is relatively short acting, it does not cause local discomfort or irritation on injection, it can be administered intravenously

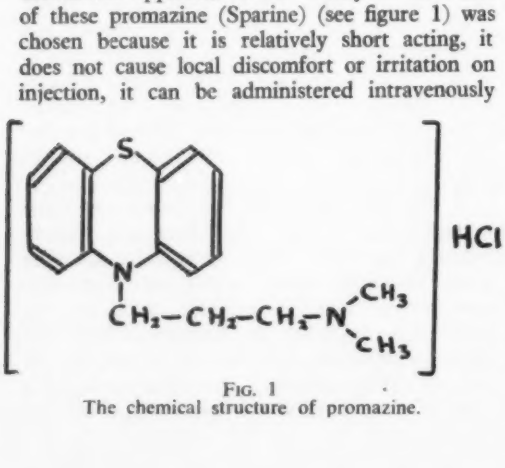

FIG. 1
The chemical structure of promazine.

and minimal toxic effects had been reported with it. A preliminary short note of the method to be described has already been published (Swerdlow and Cockings, 1958). It is the purpose of the present paper to describe in detail the technique employed and the results obtained in 160 cases and to discuss the merits of the method.

Principle.

In a few initial cases promazine was given in 25 mg doses after the regional block had been performed. This produced insufficient sedation and only when the premedication had been relatively heavy did drowsiness result. In further trial cases pethidine was given together with the promazine in a 1:1 ratio, which gave the desired sedation but frequently resulted in prolonged postoperative drowsiness. After various ratios of promazine and pethidine had been tried, it was found that the most satisfactory ratio was 2 parts of pethidine to 1 part promazine and this has been used in the latest 129 cases of the present series. Pethidine 100 mg (2 ml) with 50 mg promazine (1 ml) are diluted with 2 ml distilled water so that each 1 ml contains 20 mg pethidine and 10 mg promazine. All injections are given by the intravenous route.

Clinical method.

The premedication consists of morphine 8 to 11 mg (according to age and condition) with atropine 0.64 mg given subcutaneously 1 hour pre-operatively. Before the regional anaesthetic block is performed the pulse rate and blood pressure are measured and a nonclotting needle is inserted or an intravenous drip instituted. The initial dose of the sedative mixture is then injected, 1 ml of the mixture being given to all except the very elderly and those in poor condition, who receive 0.5 ml. The effects of this dose on the blood pressure and pulse rate are noted before the regional block is performed. After testing the height and completeness of the regional block, further doses of 0.5 to 1 ml of the mixture are given until the patient is asleep. It is essential to wait an adequate period of time after each dose to ascertain its full effect, since as long as 10 to 15 minutes may be required. In the presence of a satisfactory block and with very small doses of the mixture many patients can be tranquillized so that they lie still and

uncomplaining but, in this state, they usually retain a memory of the operation and also the surgeon cannot talk freely. We have therefore endeavoured in all cases to have the patient asleep and we try to achieve sleep before the operation commences. Overdosage will occur if attempts are made to accelerate the onset of sleep whereas, if adequate time is allowed to observe the response to each dose, a smaller total amount of the drugs will be used.

The state of sleep produced is such that the patient can at any time be awakened momentarily to answer questions. It is important that the regional block should be completely effective for otherwise the patient will respond and may be unco-operative. Occasionally the patient will spontaneously wake up for a moment and then relapse into sleep.

It is important to note the time and amount of premedication which has been administered. If the premedication has been administered considerably more than 1 hour before, rather more sedative mixture will be necessary to produce sleep, whereas if only a short time has elapsed since premedication, the pethidine-promazine mixture will have to be given cautiously to avoid undue depression later.

The pethidine-promazine mixture, especially the initial dose, causes a fall in blood pressure, which is sometimes marked. We have found that methoxamine and methylamphetamine are ineffective in reversing this hypotension but noradrenaline will raise the blood pressure when desired. Armstrong Davison (1959) has noted that atropine will reverse the hypotension caused by phenothiazine drugs and we have used atropine effectively when bradycardia was present. In general the blood pressure did not fall unduly low and we did not employ vasopressors. Blood loss, however, must be efficiently replaced and sudden movements of the patient must be avoided. In patients who had received spinal or epidural block, the blood pressure rose as the block wore off and, in practically all patients, the blood pressure had returned to satisfactory levels within one or two hours of return to bed.

The respiration was generally adequate throughout the period of sleep, but occasionally oxygenation was obviously impaired when oxygen was administered continuously or intermittently as required.

A dose of 0.5 to 1 mg of levallorphan was effective in improving oxygenation and a further similar dose of this drug was given if necessary, before returning the patient to the ward. It was noted that levallorphan had a negligible effect in reversing the hypotension. The patients almost invariably woke up on being transferred from the theatre to the ward but many relapsed into sleep on return to bed. They could, however, easily be aroused and would co-operate for any nursing or physiotherapeutic measures.

RESULTS

Table I shows the operations performed on the 160 patients here reported. It will be noted that the majority were undergoing genito-urinary operations and, as would be expected, there is a marked preponderance of elderly and aged patients (see table II). As will be appreciated, many of these patients had marked arteriosclerosis, chronic bronchitis, emphysema, hypertension, cardiac decompensation, abnormal blood chemistry and electrolyte balance. One

TABLE I
Operations performed

Operation	Number of cases
Per-urethral prostatectomy	51
Supra pubic prostatectomy	33
Cystoscopy/biopsy and/or diathermy	45
Testicular operations	2
Penile operations	9
Anal or rectal	5
Abdominal	5
Hernia repairs	5
Hand operations	2
Foot operations	2
Amputation leg	1

TABLE II
Age Range

11–20	2
21–30	0
31–40	3
41–50	7
51–60	37
61–70	50
71–80	48
81–90	12
>90	1

patient had residual hemiplegia from a previous cerebral thrombosis. The durations of the operations ranged from 10 minutes (a case scheduled for prostatectomy which actually did not proceed beyond cystoscopy) to 100 minutes. The average duration of the operations was 45.1 minutes. One hundred and fifty-two patients were male and eight were female.

The types of regional block administered are listed in table III. It will be seen from table IV that in 18 cases the local block did not completely cover the operative procedure. Of these 18 cases 7 felt only minimal discomfort and the operations proceeded satisfactorily without recourse to additional anaesthetic agents. In 2 cases a slow intravenous injection of a dilute solution of morphine enabled the operation to be completed uneventfully. In 4 cases sleep was induced with nitrous oxide and oxygen. It should be noted that in patients who have received pethidine-promazine mixture the induction and maintenance of anaesthesia with nitrous oxide and oxygen is very easy. Finally, in 5 cases a full general anaesthetic had to be administered before the operation could proceed satisfactorily.

The doses of pethidine and of promazine are given in table V. The 16 patients who received more than 70 mg of promazine were all undertaken prior to the adoption of the 2:1 pethidine-promazine ratio. It must also be pointed out that although 54.4 per cent of the patients required a total of no more than 30 mg promazine, 10 of the 12 patients aged up to 50 years required more than 30 mg promazine. In younger patients difficulty was sometimes encountered in producing sleep and repeated injections of the mixture were frequently necessary.

Of the 149 patients who did not require any additional medication continuous or intermittent sleep was achieved in 136. In the remainder a state of drowsiness only was produced. Table VI shows that amnesia for the operation occurred in the vast majority of patients and that a large number of patients did not even remember receiving the regional block.

TABLE III
Regional blocks employed

Analgesia	Number of cases
Spinal	113
Spinal + field block	13
Lumbar epidural	9
Caudal	15
Caudal + field block	1
Regional block	6
Brachial plexus block	2
Refrigeration analgesia	1

TABLE IV
Efficiency of analgesia

	Number of cases
Adequate	142
Partially inadequate	10
Totally inadequate	8

TABLE V
Total promazine and pethidine used per case

Dose of promazine (mg)	Number of cases	Dose of pethidine (mg)	Number of cases
0– 10	17	0– 20	17
11– 20	31	21– 40	38
21– 30	39	41– 60	43
31– 40	28	61– 80	31
41– 50	20	81–100	12
51– 60	1	101–120	0
61– 70	8	121–140	7
71– 80	10		
81– 90	0		
91–100	6		

TABLE VI
Amnesia

Degree of amnesia	No. of Patients	Percentage
Complete	67	
Complete for operation but remember regional block being performed	55	76.25
Partial	16	10.00
Nil	9	5.63
No data available	13	8.12

Circulatory changes.

Blood pressure. There was a tendency for the blood pressure to fall, both after the injection of the pethidine-promazine solution and after induction of the regional analgesia. The further dose or doses of the sedative mixture, administered to produce sleep, caused little further change in the blood pressure which usually remained more or less stable for the remainder of the duration of surgery.

Changes due to the initial dose of pethidine-promazine solution.

Average percentage fall in systolic pressure 11.2%.
Average percentage fall in diastolic pressure 7.4%.

The maximum drop in systolic pressure was 50 per cent (200 mm Hg to 100 mm Hg) and the maximum drop in diastolic pressure was 40 per cent (100 mm Hg to 60 mm Hg). The percentages of patients showing a marked fall in blood pressure are shown in table VII.

TABLE VII

	Systolic	Diastolic
40–50% drop in B.P	2.3%	Nil
30–40% drop in B.P.	6.9%	4.7%
20–30% drop in B.P.	10.4%	8.3%

Blood pressure changes due to regional analgesia.

Comparing the blood pressure before and after the regional block:

Average percentage fall in systolic pressure 21.2%.
Average percentage fall in diastolic pressure 17.5%.

The maximum drop in systolic pressure was 63 per cent (165 mm Hg to 60 mm Hg) and the maximum drop in diastolic pressure was 46 per cent (85 mm Hg to 40 mm Hg). Table VIII shows the percentages of patients who had a marked fall in blood pressure.

TABLE VIII

	Systolic	Diastolic
65–75% drop in B.P.	Nil	1.2%
50–65% drop in B.P.	4.2%	3.5%
40–50% drop in B.P.	3.1%	4.6%
30–40% drop in B.P.	17.7%	4.6%
20–30% drop in B.P.	20.8%	13.9%

Blood pressure changes from initial pre-operative to final "stable" state during the operation.

Average percentage fall in systolic pressure 23.4%.
Average percentage fall in diastolic pressure 23.7%.

The maximum fall in systolic pressure was 68.4 per cent (190 mm Hg to 60 mm Hg) and the maximum fall in diastolic pressure was 55.5 per cent (90 mm Hg to 40 mm Hg). The incidence of a marked total fall in blood pressure is shown in table IX.

TABLE IX

	Systolic	Diastolic
65–70% drop in B.P.	0.8%	Nil
50–65% drop in B.P.	8.7%	4.2%
40–50% drop in B.P.	22.8%	10.1%
30–40% drop in B.P.	19.7%	16.0%
20–30% drop in B.P.	24.4%	21.0%

It will be seen from these figures that the fall in blood pressure was considerably more marked with the regional block than with the promazine-pethidine injection and that in a high proportion of cases an appreciable fall in blood pressure occurred.

Pulse.

The pulse rate commonly showed a marked acceleration after the administration of the promazine-pethidine mixture. The mean percentage increase in rate caused by the initial dose was 11.6 per cent from a mean of 95 beats per minute to 106. A rise to over 120 was recorded in 38 patients. Usually the pulse rate gradually fell again to establish a more or less steady level and in 12 cases the pulse rate fell below 70 per minute. The mean overall change in those cases (133) showing an eventual steady level was not significant.

Respiration.

The overall mean respiration rate was 13.7 per minute. The lowest individual average respiration rate was 6 per minute and the highest was 20 per minute. In 88 per cent of patients the mean respiration rate lay between 10 and 16 per minute.

Complications.

There was one death, early in the series. Figure 2 shows the anaesthetic chart. A man aged 69 with advanced carcinoma of the prostate with secondary deposits had a cystoscopy, per urethral resection of prostate and evisceration of testes. At 9.30 a.m. on the following morning the patient developed circulatory collapse. Resuscitative measures were for a time partially successful but the patient's condition later deteriorated and he died about 36 hours post-operatively.

One patient, aged 83, was irritable and disorientated for some hours after operation, but thereafter made an uneventful recovery.

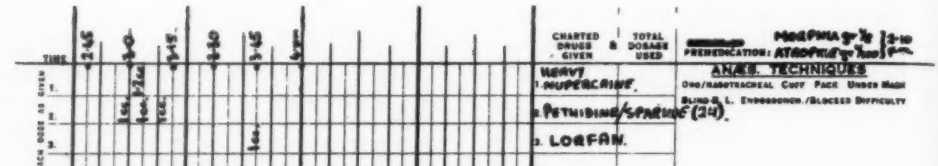

FIG. 2

Six patients developed postoperative chest complications; three of them had chronic bronchitis prior to the operation.

One patient developed severe thrombophlebitis at the site of injection.

DISCUSSION

The use of an opiate to sedate patients undergoing surgery necessitates careful individual attention to dosage. If insufficient narcotic is given the patient will be apprehensive and will remember the surgical episode. If too much opiate is given, anoxia, nausea, vomiting and hypotension may ensue. If a narcotic analgesic is to be employed, it is important to choose a drug with a good sedative action—agents like methadone are unsuitable for this purpose (Christensen and Gross, 1948; Scott et al., 1947). Scopolamine, by virtue of its amnesic properties, should be a valuable auxiliary agent but its tendency to make patients restless and unco-operative may be disadvantageous (James, 1942). At the end of the procedure a dose of a narcotic antagonist can be given if undue depression is present.

Although the barbiturates have obvious advantages as sedating agents with regional analgesia, several workers have reported disadvantages. Thus Molesworth (1944) considers that pentobarbitone gives variable results, the patient being liable to show "violent and uncontrolled reactions to the needle puncture". James (1942) finds that the patient may become restless and uncontrollable with barbiturates, and De Takats (1930) considers that the assessment of dosage is difficult. Further, the recent work of Clutton-Brock suggests a possible explanation (Clutton-Brock, 1959). The attainment of a state of drowsiness with barbiturates may be accompanied by marked respiratory and circulatory depression.

The use of general anaesthesia together with regional block subjects the patient to two anaesthetics and their dangers. In rendering the patient unconscious and depriving him of protective reflexes the anaesthetist must be responsible for the maintenance of a clear airway, etc. In younger and healthy subjects the superimposition of a light general anaesthetic to a regional block gives a negligible added risk but in the old and unfit patient a general anaesthetic may add appreciably to postoperative morbidity. As regards thiopentone, one or more small doses may often be adequate to keep a patient lightly asleep

but not infrequently "a little Pentothal" becomes a lot, particularly if the regional block is imperfect or if the operation outlasts the block. The postoperative depression associated with the use of larger amounts of thiopentone is most undesirable, especially in the older patient. The administration of a dose of thiopentone shortly after a spinal anaesthetic is not without danger.

Various combinations of tranquillizers and narcotics have been employed by different workers to supplement regional analgesia. Frankis Evans (1954) administered chlorpromazine 30 mg with pethidine 30 mg intravenously before epidural anaesthesia and then after performing the block he gave thiopentone 250 mg. However, two patients developed pulmonary emboli after the use of this technique and he no longer employs chlorpromazine with epidural anaesthesia

Lahayville (1954) injected a mixture of pethidine and promethazine 1 hour pre-operatively and then gave diethazine 15 minutes before the operation to render the patient somnolent during epidural anaesthesia. He found that if epidural anaesthesia started to wear off prematurely, a dose of diethazine or pethidine would permit completion of the operation.

Adelman et al. (1959) have recently reported the supplementation of spinal anaesthesia with 25 mg promethazine alone intravenously. When this is insufficient to still the patient, they give intravenous doses of pethidine 10 mg with promethazine 10 mg until satisfactory sedation is obtained. They claim absence of hypotension and tachycardia. Zettler (1954) gives a mixture of chlorpromazine 50 mg, promethazine 50 mg, and pethidine 100 mg 2 hours prior to epidural anaesthesia. This is repeated 1 hour pre-operatively provided the blood pressure is still above 100 mm Hg. Zettler noted the slow, deep respiration and the low but steady blood pressure. He found that the dose of local anaesthetic required for epidural anaesthesia was reduced, an observation also reported by Schultze (1954). Schultze and Schafmeister (1955) administer promethazine 50 mg with chlorpromazine 75 mg 2 hours pre-operatively and pethidine 100 mg intramuscularly 1 hour before operation. In addition 73 per cent of their patients were given up to 500 mg of hexabarbitone and 15 per cent received more than 500 mg. They note prolonged postoperative drowsiness and sleep.

Morel-Fatio (1955) gave a combined diethazine/pethidine injection before infiltration with lignocaine for facial surgery but a prolonged regime of barbiturates, belladonna derivatives and promethazine was also given pre-operatively.

Sprague (1957) administered pethidine 25 to 50 mg with scopolamine 0.32 mg and promazine 25 mg, to sedate mothers undergoing delivery under saddle block anaesthesia, with satisfactory results.

In the present work the dosage of both tranquillizing and narcotic drugs has been smaller than that used by most of the previous workers and sleep rather than sedation has been the objective. However, the present patients were of a higher age group and such patients were found to require less supplementary medication than younger subjects. Indeed Eger and Keasling (1959) consider that in old and senile patients neither pentobarbitone nor meprobamate has much advantage over a placebo for producing sedation with regional analgesia.

The degree of amnesia associated with the use of tranquillizer-narcotic mixture is remarkable, a finding which was also noted by Zettler (1954).

The present method is by no means perfect nor are the drugs ideal, but it has certain advantages over the techniques which have been previously employed to supplement regional analgesia. In successful cases sleep and amnesia are achieved with very small doses of two relatively nontoxic agents without resorting to the use of full surgical anaesthesia. The use of the intravenous route permits, to some degree, the titration of dosage and some precision as to the time of onset of sleep. The patient can, if necessary, be awakened temporarily during the operation to provide information or to co-operate in other ways should this be desirable. The use of a phenothiazine derivative should reduce the incidence of nausea and vomiting (Morris, Matthews and Moyer, 1954). However, it must be noted that in the present work transient nausea and retching occurred occasionally shortly after the injection of the initial dose of promazine mixture. This could be adequately assuaged by the administration of oxygen or instruction to breathe deeply.

On the other hand, the technique has a number of undoubted disadvantages. It demands the greatest individual care and attention in induction of sleep, in maintenance and in the immediate postoperative period. A considerable period of time may sometimes elapse before the patient is asleep and sleep and drowsiness may greatly outlast the surgical procedure. The method is therefore unsuitable for shorter procedures. Serious falls in blood pressure may occur and, less frequently, some impairment of oxygenation. Finally if the regional block proves inadequate the patient will become restless and unco-operative.

In conclusion, it must be pointed out that the problem at issue is how best to sedate adequately and safely the patient for whom regional analgesia is considered to be the method of choice. We consider that none of the methods described to date is uniformly satisfactory. In the younger, relatively fit patient undergoing surgery under regional analgesia, supplementation with some form of light general anaesthesia is probably the soundest policy. In the elderly patient, however, there is a place for a technique such as that described above.

SUMMARY

A brief historical review is given of the methods which have been employed to sedate patients undergoing surgical operations under regional analgesia.

A method of sedation using a mixture of pethidine and promazine is described and the results obtained in 160 patients are analyzed. Satisfactory results were obtained in a high percentage of older patients. The advantages and disadvantages of the method are discussed.

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AN OBSTETRIC ANAESTHETIC TABLE

BY

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METHODS of anaesthesia in obstetrics have recently been under review (*Lancet*, 1955; *British Medical Journal*, 1956; Hodges et al., 1959). In this field of anaesthesia that which sets out to be a minor procedure may at any time develop into a major anaesthetic emergency. The equipment usually provided is not always readily available or adequate for such an emergency.

Shown in the photograph is a set-up which has been found satisfactory for handling such cases at St. Thomas's and the General Lying-in hospitals during the past two years.

A standard anaesthetic table top is replaced by one of $\frac{1}{8}$-inch perspex which is suitably divided by strips of the same material into separate compartments. A polyvinyl cover is provided so that items are kept clean between cases. A plan photograph of the arrangement is kept on the machine so that nursing staff can easily check between cases that no item is missing.

The system has proved popular with the nursing staff and has helped considerably to reduce the delay in providing anaesthesia for these cases.

The original table tops were made in the Surgery Department of St. Thomas's Hospital. Copies can be obtained to order from Matburn Ltd., 25 Red Lion Street, London, W.C.1.

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Suxamethonium
d-Tubocurarine
Ergometrine
Neostigmine
Atropine
Thiopentone
Swabs
I.V. needles and cannulae
Cuffed tube and stilette
Lubricant
Connections
Syringe
Spencer-Wells forceps
Gordh needles
10 ml and 2 ml syringes
Laryngoscope

Brit. J. Anaesth. (1959), **31**, 554

MODIFIED BEAVER RESPIRATOR: THE APPLICATION OF NEGATIVE PHASE

BY

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THAT intermittent positive pressure may adversely affect the circulation under certain circumstances, notably when there is hypovolaemia, is widely recognized (Maloney and Handford, 1953; Brecher, 1956) and with many automatic ventilators it is possible to provide a degree of "negative pressure" during the expiratory phase to combat this tendency to circulatory depression.

Many of these machines are complex or expensive, so a simple adaptation of an available ventilator—the Beaver mark I—was made to provide this "negative phase" for use in routine anaesthesia.

The machine used was the production model made by the British Oxygen Company in 1953 and differs somewhat from the prototype originally described by Beaver (1953). It was supplied to many hospitals by the Ministry of Health for treating poliomyelitis cases.

Both the designer (Beaver, 1955) and Burchell (1957) have previously described modifications to produce a negative phase, but it is suggested that the present device is simpler. It can be attached to any closed circuit anaesthetic apparatus provided that, as is customary, the rebreathing bag of the latter is readily detachable.

THE APPARATUS

The apparatus is shown in figure 1. The wide-necked confectionery jar of 5 litres capacity (costing 3*s.* 6*d.*) contains a standard rebreathing bag which holds about 2.5 litres. This bag is connected to a length of corrugated tubing and replaces the rebreathing bag on the anaesthetic machine when the ventilator is in use. The existing screw-on lid of the jar is reinforced by a brass plate and is drilled to take two 1-inch diameter brass tubes. (This is the only part of the conversion for which workshop facilities are essential.) One tube is connected to the anaesthetic apparatus above and to the bag below as described. The other opens below into the bottle—outside the bag—and its upper end is connected to the delivery tube from the ventilator. The B.O.C. non-return valve supplied for this tube is not required. This assembly can easily be taken apart for cleaning and sterilizing.

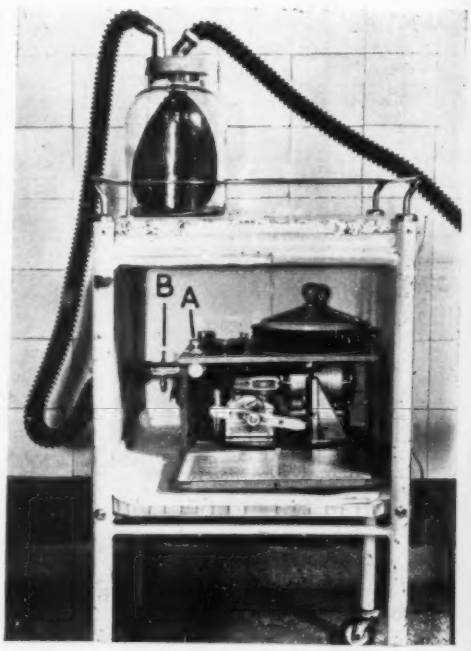

FIG. 1

The converted apparatus. The front of the box has been removed to show the position of the subsidiary controls.

Although the electric motor and the gearing of the Beaver ventilator are reasonably silent, the air valves on the cabinet are not, and also the bellows make an appreciable crackling noise when expanded against resistance. To render the machine acceptable for use in the operating theatre, therefore, it has been enclosed in a box lined with sound-absorbent material, and mounted on thick sorbo pads.

A hole has been drilled in the floor of the box underneath the existing hole in the machine cabinet to allow air to enter, and vents have been left at the top corners.

There has been no trouble with overheating, and the standard of silence compares very favourably with that of many other ventilators in common use.

THE WORKING OF THE MACHINE

During inspiration air from the electrically driven bellows on the machine enters the bottle and compresses the bag containing the anaesthetic gases, thus inflating the patient's lungs. Surplus air from the bellows blows off from the valve on the machine in the usual way.

In the expiratory phase, the bellows of the machine fills, partly from the air inlet valve on the ventilator, but chiefly from the bottle, thus tending to produce a negative pressure inside the bag and anaesthetic circuit.

Whether or not this negative pressure is produced depends mainly on the amount of gas in the anaesthetic circuit. This is controlled by the flow of fresh gases and by the usual expiratory valve in the closed circuit.

Using the customary closed circuit with a leak, and a gas flow of about 3 litres per minute, this valve can usually be adjusted within a few seconds. Often the setting used for the previous manual compression of the bag is satisfactory.

An essential aid to this adjustment is a pressure gauge. An air speed indicator registering up to 160 knots is very satisfactory for this purpose. This is connected by sphygmomanometer tubing to the side arm of an Ayre's T-piece in the catheter mount. The existing gauge on the machine is ignored.

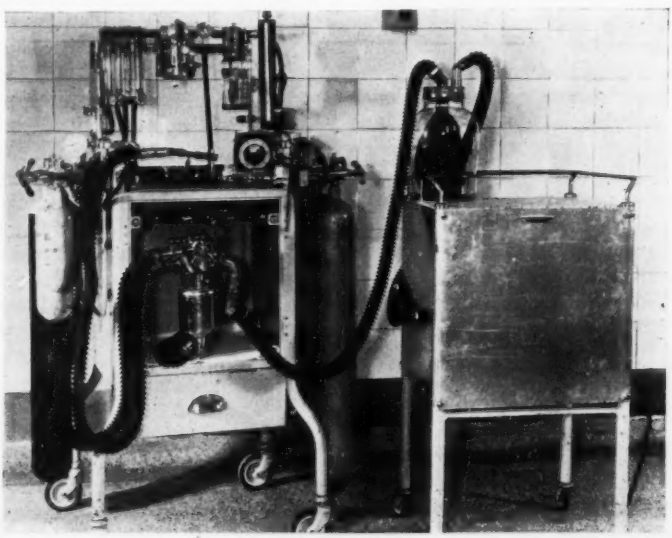

FIG. 2

The ventilator connected to a standard anaesthetic machine, showing the pressure gauge and modified catheter mount.
Warning. Although the cyclopropane cylinder is shown in this photograph, this apparatus is NOT suitable for use with explosive anaesthetics.

THE MACHINF IN USE

After the induction of anaesthesia, the endotracheal tube is attached to the special catheter mount connected to the pressure gauge, and note is taken of the respiratory movements and of the "feel of the bag" in the normal way. These are then correlated with the pressure shown on the gauge. In a straightforward case this would be, say, +2 to +15 cm water. The rebreathing bag is then disconnected and replaced by the corrugated tube attached to the bag in the bottle (fig. 2) and the pump is switched on. The expiratory valve on the anaesthetic circuit is then adjusted to produce a negative pressure of about −2 to −4 cm water, and in the case just quoted the inspiratory pressure would probably be between 10 and 15 cm water. A typical pressure tracing is shown in figure 3.

The negative pressure can easily be abolished, if required, by closing the valve or increasing the fresh gas flow.

The possible fallacies of deducing the respiratory exchange solely from pressure changes must be borne in mind and the patient's chest must be observed to see that it moves adequately.

This method of assessing ventilation does not differ materially from that used in manual compression of a rebreathing bag, and it takes only a moment to revert to the latter method of inflation when this is felt desirable.

A Wright ventilation meter was employed on many early cases, but its routine use was discontinued as ventilation was always considered to be more than adequate except in the rare case where a very high inflation pressure—over 25 cm water—was required to inflate the chest.

For cases of this kind, the necessary high inspiratory pressure may be produced by using adhesive tape to occlude partially the "blow-off" valve (A in fig. 1) on the ventilator cabinet.

The corresponding air inlet valve may be similarly occluded to increase the negative pressure during expiration, but this has very seldom been necessary, and indeed is not devoid of risk (Lynch, Levy and Kent, 1959).

For small patients it is possible to reduce somewhat the effective ventilation produced by the machine by opening the tap (B in fig. 1) and bleeding off air through the side arm. (The original purpose of this fitting was to admit oxygen to enrich the air supplied by the ventilator.)

It should be emphasized that these three adjustments are only seldom required; indeed the need to silence the machine has rendered them relatively inaccessible. Normally the expiratory valve on the anaesthetic circuit is the only control that needs attention.

ADVANTAGES OF THE MODIFIED MACHINE

No originality is claimed for this conversion: the "bag in bottle" principle is employed in many ventilators (Mushin, Rendell-Baker and Thompson, 1959).

It is described partly because it has proved most successful in routine anaesthesia, and partly in the belief that there are many Mark I Beaver ventilators which are not fully utilized. This machine is devoid of the controls for adjusting the rate, the stroke volume and the inspiratory-expiratory ratio, which, together with other refinements are provided in the Mark II design.

The absence of such controls has not proved a disadvantage in practice; indeed the reverse is the case, and the rapidity and ease with which this apparatus may be adjusted has proved one of its

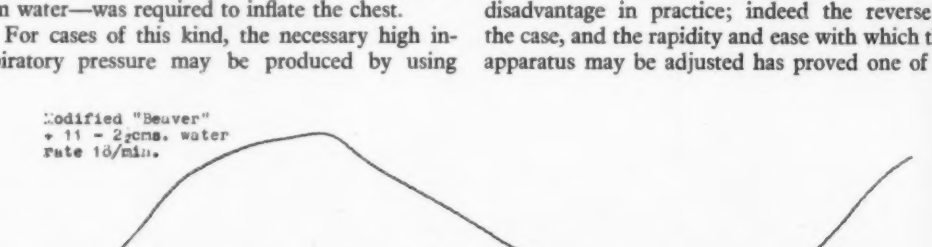

FIG. 3

A typical record of pressure changes at the catheter mount. This was made during a laparotomy on a 10-stone woman aged 53.

greatest assets. This simplicity of adjustment is obtained only at the expense of causing an appreciable degree of overventilation in the majority of patients. This is not considered undesirable, for deliberate overventilation is a recommended, and widely used, adjunct to anaesthesia (Geddes and Gray, 1959). It would appear to cause clinically insignificant changes in the acid base balance over the period of an average surgical operation (Papadopoulos and Keats, 1959). Using this machine coupled to a standard anaesthetic apparatus with proximal unidirectional valves, and the usual fairly distensible corrugated tubing, no ill effects have been observed in some hundreds of cases including a few having operations of 9 hours duration.

Indeed, one has perhaps had the impression that normal respiration is more easily re-established after prolonged ventilation with a machine with "negative phase", than after ventilation by manual compression of the bag.

No audible wheezing during expiration, as reported by Lynch, Levy and Kent (1959), has been observed. These authors used a considerably greater negative pressure (− 5 to − 10 cm water) than the − 3 cm water most commonly employed in the present series.

The Beaver Mark I ventilator is supplied with a fixed respiratory rate of either 14 or 18 a minute. Both types have been used and have given satisfactory and completely reliable service over the past two years. However, the machine with the faster respiratory rate has been preferred, as with it the gas flow is more rapid and overventilation more certainly achieved.

The smoothness of expiration seen with this machine is a pleasing minor feature, and compares favourably with the noticeable "jerk" produced by some other ventilators in common use.

The types of case where a negative phase has been most appreciated have been:

(1) Abdominal surgery where major haemorrhage was encountered.

(2) In head and neck surgery, where the collapsed veins provide excellent operating conditions.

(3) Cases with "fixed chest" or obesity requiring high inflation pressures.

(4) Certain cases where hypotension was deliberately induced, usually with halothane.

(5) Poor risk cases.

The knowledge that the ventilator does not materially impair the circulation is very reassuring, and enables a fuller attention to be given to the assessment of the circulation and to the control of blood transfusions.

SUMMARY

A simple and inexpensive modification of the Beaver Mark I ventilator is described. It produces a "negative" (subatmospheric) pressure during expiration when used in conjunction with a standard closed circuit anaesthetic machine.

The merits of this combination are briefly outlined and its successful use in clinical anaesthesia is reported.

ACKNOWLEDGMENTS

I am indebted to Mr. D. McVay, our anaesthetic technician, for the constructional work, and to the photographic department of the Middlesex Hospital for the illustrations.

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Brit. J. Anaesth. (1959), **31**, 558

MODIFIED ANGLE PIECE FOR CHILDREN'S ANAESTHESIA

BY

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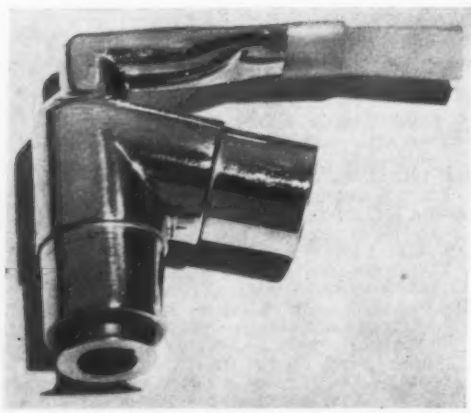
IN an article (*Brit. J. Anaesth.*, 1958, **30**, 182), a modification to standard facepieces was suggested to obviate the disadvantages of deadspace and valve pressure during anaesthesia in children where intubation was not required. Though perfectly satisfactory, only a limited number of masks could be modified, and these were often mislaid and not available when required.

A standard angle piece was therefore modified as shown in the accompanying photograph, so that it could be used with any mask and yet retain the benefits of the original system. Into the vertical end of the angle piece when in use, a tube of $\frac{3}{8}$ inch internal diameter and $\frac{1}{2}$ inch external diameter is soldered, the distal end of which bears the latex flow-indicator. Fresh gases from the machine enter the horizontal arm of the angle piece and enter the mask round the tube. Expired gases and excess flow from the machine leave via the tube in the vertical arm of the angle piece, and escape through the latex tube.



Modified Angle Piece

The cross section of the expiratory tube is 0.11 sq.in., equivalent to the cross section area of a No. 9 endotracheal tube, and the inspiratory portion of the angle piece has a cross section area of 0.25 sq.in. As the energy required for the passage of gas through this angle piece is supplied by the flow of fresh gases from the machine, it is not thought that such a system would increase resistance to respiration in children for whom it is designed.

The angle piece is shown in the photograph as bearing a flange on the mask end of the expiratory tube. This was designed to spread the incoming gases around the mask, but has had to be omitted since masks with a rubber instead of a metal collar came into use.

This angle piece may be obtained from A. Charles King Limited, and the latex valve is made from $\frac{1}{8}$-inch Pauls latex tubing. This is creased like a trouser leg at its end by drawing thin lines with latex solution at opposite points on the circumference and pinching the tube together. This encourages the valve to collapse properly when necessary.

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Brit. J. Anaesth. (1959), **31**, 559

A RIPPLE MATTRESS FOR THE OPERATING TABLE

BY

DAVID ZUCK

Department of Anaesthesia, Chase Farm Hospital, Enfield

IN an attempt to prevent venous stasis in the dependent parts, a "ripple" mattress has been adapted for use on the operating table during long operations. The "ripple" mattress, which has had a proved success in the prevention and treatment of bed sores, consists of two sets of interdigitating tubes which are inflated and deflated alternately. The pressure-bearing areas of the patient are thus being changed continuously, and in addition to minimizing venous stasis, the mattress may also prevent the generation of bed sores during operation.

FIG. 1
The mattress and the motor

The mattress is made of antistatic rubber and can be tailored to fit any operating table. It can be used in the Trendelenburg position, with the knees flexed. The motor is very quiet.

The mattress is sent to the ward on top of the trolley canvas, and the patient lies directly on it. Ideally the patient should continue on such a mattress in bed until able to move freely.

The mattress has been in use for nearly all major cases in one operating theatre for about a year, and none of these patients developed venous thrombosis in the legs. This is not regarded as of significance, however, since it is appreciated that the value of this sort of measure cannot be proved except in a very large series of cases over a number of years. The method is at present suggested as possibly being of value during operations lasting more than a short time.

Since submitting this paper for publication the writer has been informed that a similar mattress is already available in the United States.

ACKNOWLEDGMENT

The equipment was supplied by Talley Surgical Instruments Ltd., 37a New Cavendish Street, London, W.1.

I am indebted to Miss B. Whiteley of the Medical Photography Department of the Enfield Group of Hospitals for the photograph.

V LATIN AMERICAN CONGRESS OF ANAESTHESIOLOGY

We have received information that the V Latin American Congress is to be held in conjunction with the VIII Mexican Congress of Anaesthesiology at the University City in Mexico, D.F., during November 1960. The Organizing Secretary invites those interested from this country who would like to attend this Congress to submit their papers to him at the following address:

DR. ENRIQUE HULSZ S., Apartado Postal 13649, Admon 45, Mexico 1, D.F.

Brit. J. Anaesth. (1959), **31**, 561

POSTINTUBATION ULCER OF THE LARYNX

Report of a Case

BY

VICTOR CAMPKIN

Queen Elizabeth Hospital, Birmingham

CONTACT ulceration and some sessile and pedunculated laryngeal lesions may all occur in the pathogenesis of postintubation granuloma, an uncommon complication of endotracheal intubation. Epstein and Winston (1957) reviewed sixty-five cases and thought that the condition is becoming commoner owing to the more frequent employment of endotracheal intubation in recent years. Nevertheless, published reports of cases are comparatively few, mainly because the onset of symptoms may be delayed for weeks or months and so escapes the notice of the anaesthetist and of the surgeon at his follow-up clinic.

The case reported here is of interest in that the onset of hoarseness, the common presenting symptom, was unduly delayed, and persisted with occasional remissions for some years before diagnosis and treatment.

CASE REPORT

In February 1953, Mrs. J. M., aged 44 years, was admitted to the Royal Victoria Hospital, Belfast, for removal of a large nontoxic goitre. At operation a subtotal thyroidectomy was performed under general anaesthesia with endotracheal intubation. No details of the type or size of tube used are available but anaesthesia and operation were uneventful. There was no evidence of recurrent laryngeal nerve damage post-operatively, nor did she complain of hoarseness at the follow-up clinic.

Some ten months later the patient noticed that her voice had become hoarse and this persisted with occasional remissions to date.

In March 1959 she was admitted to the Queen Elizabeth Hospital, Birmingham, after a diagnosis of bilateral carpal tunnel syndrome had been made. On March 14, 1959, division of the right carpal ligament was performed under general anaesthesia with orotracheal intubation. The duration of the operation was 35 minutes and no laryngeal abnormality was noticed, probably because the patient had not mentioned her persistent hoarseness.

In July 1959, she was readmitted for operation on her left wrist. She now complained of hoarseness, and stated that it had become worse following her previous operation in March. At operation a careful inspection of the glottis was made after induction of anaesthesia and an oval ulcer was seen to involve the posterior commissure and the vocal process of the left arytenoid cartilage. In addition there was a small sessile lesion arising from the tip of the vocal process.

The patient was subsequently referred to the ear, nose and throat department, where biopsy of the sessile lesion was undertaken. The pathological report stated: "Squamous cell papilloma. No evidence of malignancy."

DISCUSSION

The long history and histological report excluded malignancy in this case and benign tumours of the larynx are not associated with coincident ulceration. The sessile lesion arising, as it did, from the ulcer edge was probably an excessive proliferation of squamous epithelium as part of the healing process.

It seems reasonable, therefore, to incriminate endotracheal intubation as the cause of this lesion. Postintubation granuloma is more common after thyroidectomy than after any other surgical operation. This is probably due to the position of the head during anaesthesia. With the head and neck hyperextended, usually by placing a pillow or sandbag under the shoulders, an endotracheal tube in position will press maximally upon the posterior commissure and vocal processes at the glottis. Howland and Lewis (1956) cite this as an important aetiological factor and describe twenty-one cases of intubation granuloma following thyroidectomy out of a total of thirty-five. Of the sixty-five cases analyzed by Epstein and Winston (1957) eight followed thyroidectomy. Howland and Lewis (1956) also suggest that intubation granuloma is more common in females because of the higher incidence of thyroidectomy and the smaller size of the female larynx.

Most authors agree that static pressure is a more likely cause of intubation lesions than damage inflicted during attempts at intubation, particularly since relaxant agents render the pas-

sage of an endotracheal tube relatively easy and atraumatic. Prolonged pressure of a semi-rigid tube will cause ischaemia but in one case reported by Wylie (1950) the tube was in situ for only 15 minutes. Coughing and straining on a tube might also serve to produce the initial abrasion of the larynx which may then progress to ulceration and granuloma formation.

Despite the relatively few cases of this condition described in the literature, unpublished data suggest that the incidence may be as high as 4 per cent following intubation (*Brit. med. J.*, 1957). Its recognition depends upon the development of symptoms within a reasonably short period postoperatively. Both sore throat and hoarseness are not infrequent after endotracheal intubation, 23 per cent developing one or other of these symptoms in a series of 521 patients interrogated by Wolfson (1958) and 10.9 per cent of patients had symptoms persisting for more than two days. Any postoperative hoarseness lasting for more than a week should therefore be investigated by indirect laryngoscopy and the presence of contact ulceration excluded. Conservative treatment at this stage, involving complete vocal rest, will usually effect a cure. It would seem that the majority of patients who develop symptoms only after a delayed interval will continue to escape recognition by the anaesthetist.

To prevent this complication the use of rough, too rigid or too large endotracheal tubes should be avoided. Portex or flexo-metallic tubes compress the posterior glottis less and the avoidance of excessive extension of the head and neck during thyroidectomy might also serve to reduce the incidence.

SUMMARY

A case of postintubation ulcer of the larynx is described. The aetiology of this condition is briefly discussed with particular reference to the role of posture of the head and neck during thyroidectomy.

ACKNOWLEDGMENT

I would like to thank Mr. E. A. Turner, F.R.C.S., Consultant Neurosurgeon, The United Birmingham Hospitals, for permission to publish details of this case.

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Automatic Ventilation of the Lungs. By William W. Mushin, L. Rendell-Baker and Peter W. Thompson. Published by Blackwell, Oxford. Pp. 349; illustrated. Price 47*s.* 6*d.*

The number of automatic ventilators has become so large, their variety so bewildering, and their descriptions so widely scattered, that most anaesthetists have given up the struggle to remain *au fait* with the subject.

It is pleasant for them to realize—as they must on looking into this book—that there is now a compendium of up-to-date information at their disposal; and Professor Mushin and his co-authors have earned their gratitude.

The authors start with a consideration of the physiological aspects of controlled respiration. This deals briefly with different types of pressure pattern, with elastic and nonelastic resistance, and with the cardiovascular effects of imposed patterns of ventilation. This is in general clear and informative, though on one occasion "compliance" is confused with its opposite. In dealing with the estimation of ventilatory requirements, more stress is laid on nomograms and tables than on biochemical measurements. Various types of ventilation meter are described, and timely warning is given of the error in their use which may arise from changes in the volume of connecting tubes.

There follows an analysis of pressure generators and flow generators and of the different means by which the change-over from one phase of respiration to the other is brought about.

The main part of the book consists of a systematic description of about fifty automatic ventilators. For each, there is a description of the working parts, with a diagram and, in many cases, a photograph, followed by a "functional analysis". In this, each machine is classified with respect to the means by which each phase is started, maintained and terminated. Devices for manual operation and different types of inflating valve are also considered.

So clear are the descriptions and the diagrams that they afford the reader as good an idea of each machine as he could gain from painstaking work with a screwdriver and spanner and without the embarrassment of having to dispose of the pieces left over after re-assembly.

The book will certainly be very widely consulted, and it is so clearly written and so well produced that to consult it is a pleasure.

Ronald Woolmer

Handbook of Balanced Anesthesia. By Sylvan M. Shane. Published by Lowry & Veloz, Baltimore (1958). Pp. 272; illustrated. Price $7.85.

Sylvan M. Shane has attempted to design a safe "balanced" technique for dentists, obstetricians, anaesthetists and nurse anaesthetists. A single small dose of a short-acting barbiturate (e.g., 16 ml 2.5 per cent thiopentone is an average adult dose) produces unconsciousness, and the patient then breathes a mixture of nitrous oxide (1 litre/min), oxygen (2 litres/min) and cyclopropane (400 ml/min), via a semi-closed CO_2 absorption system. After 3 minutes plane I of the surgical stage is reached, and remains so long as the mixture is inhaled; this technique can be used for any type of surgery regardless of the age of the patient, and there are no known contra-indications. Shane stresses that adult patients will not vomit with this method; however, children under the age of 12 years may eructate gastric juice and develop laryngeal spasm: they must, therefore, be intubated, especially before abdominal surgery. Shane admits that muscle relaxant drugs may be needed with this technique.

The section on intubation favours suxamethonium, but omits to give guidance on how to position the patient. It simply states, "remove the mask, insert the laryngoscope, expose the cords"; evidently it is considered more important to mention the difficulties of intubation before the relaxant era. These were only decreased somewhat, according to Shane, by the "Pentothal-curare" technique in which a massive dose of thiopentone was combined with a "near

paralysing" dose of d-tubocurarine. Shane claims that "the interval prior to the assumption of spontaneous respiration would sometimes extend to the point of bag-squeezing fatigue. And there was more than one anaesthesiologist who wondered if the patient would ever resume respiratory movements of an amplitude compatible with relinquishing the increasingly tense grip on the rebreathing bag".

His statement that the open drop ether method is dangerous and obsolete and that nitrous oxide, oxygen ether is almost as dangerous, is an opinion which will not be shared by British anaesthetists. Any method can be dangerous in the hands of one who is not properly taught, and the inclusion of irrelevant material clumsily presented can only do harm; for instance on page 191 Shane writes, "there are few anaesthesiologists who enjoy being conscious during the erratic hours which obstetrical anaesthesia entails".

Concerning relaxant drugs, Shane suggests that a young, healthy, muscular male may require as much as 120 mg of gallamine. He goes on to state that if further relaxation is needed for peritoneal closure it is safer to use intermittent doses of suxamethonium irrespective of whether the patient is a good or a poor risk. He states that after excessive doses of relaxant drugs their ill effects are seldom noted in the operating theatre, and that a catastrophe may occur about 20 minutes after removing the mask when the patient is out of the anaesthetist's immediate care. Return of muscle tone after the injection of an antidote like edrophonium is considered by Shane to be misleading. If he entertains the idea that the edrophonium dosage is insufficient he does not mention it.

At the beginning of this work there is a plea that the reader should "appraise or condemn the book entire, and not a few particular phrases". Unfortunately there are many examples of material very poorly presented. For example, in considering the risk of anaesthesia for the patient who has had a recent coronary occlusion, Shane states: "We know of no way to protect these individuals other than by interrogation." The plea continues: if the readers "would search into the designs of the author, they can do it in no other way so completely as by searching into the designs of the work". Evidently the main design is to popularize the S-A technique which is mentioned in 64 out of the 260 pages, excluding the bibliography and index. The largest number of references in one page is six.

Shane's work, poor as it is, raises the question, can the technique be safely and effectively managed by the "anaesthetically inexperienced personnel" for normal women in labour? A further and more detailed trial by unbiased observers would be revealing.

R. P. Harbord

Printed in Great Britain by JOHN SHERRATT & SON, Park Road, Altrincham

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